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BIOMEDICAL RESEARCH

HEARING

BEFORE A

SUBCOMMITTEE OF THE
COMMITTEE ON APPROPRIATIONS
UNITED STATES SENATE

ONE HUNDRED FIRST CONGRESS

SECOND SESSION

SPECIAL HEARING

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BIOMEDICAL RESEARCH

WEDNESDAY, MARCH 28, 1990

U.S. SENATE,
SUBCOMMITTEE ON LABOR, HEALTH AND HUMAN SERVICES, AND EDUCATION, AND RELATED AGENCIES,
COMMITTEE ON APPROPRIATIONS,
Washington, DC.

The subcommittees met at 10:03 a.m., in room S–128, the Capitol, Hon. Tom Harkin (chairman) presiding.

Present: Senators Harkin, Hollings, Bumpers, Adams, Specter, and Stevens.

NONDEPARTMENTAL WITNESSES

OPENING REMARKS OF SENATOR HARKIN

Senator HARKIN. Good morning. The subcommittee will come to order. The benefits of medical research are undisputed and supporters are many. In fact, this committee, I think, has placed a very high priority on biomedical research. We have doubled the funding for NIH since 1982, during the time when the discretionary spending in our subcommittee only went up by 14 percent. So I think support on this subcommittee and indeed the entire Appropriations Committee has been strong during this period of time.

In fact, our public witnesses, starting last week and this week, of 150 witnesses, 85 are there testifying on NIH and biomedical research topics, 85 of the 150 public witnesses.

During the testimony we have heard of downward negotiations, sometimes as high as 20 percent. We have heard of the declining number of new grants being awarded; declining funding rate, which this year will be 24.2 percent; research opportunities not funded. We have heard of the needs for attracting young people into research careers, the lack of funds we have for that, and we have heard the request for a $9.2 billion funding level, which is $1.3 billion over the President's request and $1.8 billion over last year's.

We are here today to discuss the challenges facing us in the nineties: Where are we now in our research efforts; how medical research touches the lives of Americans; what we can anticipate for the future in terms of building our success, our international stature and competitiveness in the biomedical research area.

More and more, this committee has to take a larger view of the entire research picture: Training, grants, clinical trials, centers,

and construction. They are all recognized as an integral part of the research enterprise.

Research like a chain is only as strong as its weakest link. We look forward to today's testimony and to all of your insight into this important area. We are at a crossroads in research, and we have to make some very important decisions as to what we are going to do in the 1990's.

I, first of all, want to thank Senator Hollings, who initially requested this special hearing on this topic to investigate these areas and to bring to light some of the important testimony you are going to have today. It will serve an important purpose. I want to thank all of the witnesses for sparing the time to be with us.

I have other commitments this morning. As I said, it was Senator Hollings who was the sparkplug to get this hearing going and to move it along. I wanted to be here because of my intense interest in this area, too. I am basically going to turn it over to Senator Hollings, and I am going to stay here for a while, until I have to run to, if I am not mistaken, Agriculture.

I will just turn it over to the distinguished Senator from South Carolina.

OPENING REMARKS OF SENATOR HOLLINGS

Senator HOLLINGS [presiding]. Thank you very, very much, Mr. Chairman. We appreciate your interest, your commitment and your leadership. Right to the point, on the matter of trade, working in that discipline also, I just got on my desk before I walked over here, an article by our friend Dr. Robert Reich. I say our friend because we worked very closely when he was at the Federal Trade Commission. Dr. Reich's article is entitled "Who Is Us?" and it deals in the field of trade.

He rationalizes that so long as an industry, whether it be Japanese, American, Canadian, or whatever, as long as it employs jobs in America then we should all go away and be happy.

I strongly differ with that thinking. The countries who really invest the money in the research and development are the ones who are going to attract the brains that you see at this table to their graduate schools. I see our competitors in Tokyo put up $19 billion 2 years ago to start 19 campuses in graduate work. As a result, they will attract everybody to research in Japan; they will attract everybody to development in Japan, and yes, we can have the assembly jobs in America, but that is not going to win us our economic security or maintain for us our leadership. We are moving from the cold war victory now to the trade war competition.

In that light, the Federal commitment in biomedical research has been really lagging. We always talk about how we have got to be more productive, more competitive.

Everybody outside of this town is more productive and more competitive. It is we in Washington who are not producing and not competing for a single NIH senior research scientist in the last 10 years. We haven't been able to bring on such a person because we haven't been able to afford one. A researcher trainee, to start is, what, $17,000? A secretary gets more than that. [Laughter.]

You get a doctor, a fellow who has a master's and a doctorate—he has been in school for a good 8, 10 years, with education loans to repay. He owes everybody, the family and what-have-you, and then comes to work for $17,000. He has to at least think of how the bills are being paid so the private sector takes him off for $73,000.

The Federal investment in biomedical research has just really been totally inadequate and these fine witnesses that we have today, I think, will draw a good picture for us so you and I can sell our apples on the floor of the Senate.

Thank you, too, for your setting this whole thing up for us and your leadership.

Senator HARKIN. You were the one that started this originally. I appreciate it.

OPENING REMARKS OF SENATOR STEVENS

Senator STEVENS. Senator, really, I heard that we were supposed to have a hearing. We have been concerned with this endeavor of affairs, too, because the problem, it looks like, is that more and more of the research is being done by nonprofit corporations and organizations who are hiring the same people that would have been hired at NIH.

The one constraint that we need to get around is the restraint of the salary level, the payments made to attract researchers. It is a very complex problem. I am interested to hear what the witnesses have to say. But it does seem to me that part of the difficulty is in the level of compensation we can pay.

On the other hand, it may be that the costs of running those nonprofit corporations is taking more out of the system than it should be taking in order to meet those payments. We can't even think about how much it costs to run a nonprofit corporation today, the staff and what-not. It is support for the same research that could have been done in NIH. I would like to hear some comments about that.

There has to be some way to determine what entities we are going to provide the level, the range, to them; also, how are we going to give grants to individuals who are really employed by nonprofit corporations who are actually doing the work that we thought was going to be done at NIH in the buildings we have already built and the staff is supposed to be maintained for the system.

I hope you won't misunderstand me. I am not against the nonprofit effort to do the job, because we can't do it under the present system in the NIH. It is one of those complex things we need to resolve or at least tangle with. I am not sure you can resolve it around here.

STATEMENT OF DR. DENNIS BUSCH, BAYLOR COLLEGE OF MEDICINE, PRESIDENT, AMERICAN ASSOCIATION FOR CANCER RESEARCH

Senator HARKIN. Did you all hear that? Maybe we can talk about that. We have our first panel, Dr. Harris Busch from Baylor College of Medicine; Dr. Willa Hsueh from the LAUSC Medical Center; Dr. David Korn from Stanford and Dr. Steve Ryan from the University of Southern California School of Medicine.

We are delighted to have you here, and not in any order of priority. I guess maybe by alphabet, then, alphabetic order. Dr. Busch, welcome, and please, all of you who have come this distance, thank you for taking your time and effort to be here. We appreciate it. All of your statements will be made a part of the record in their entirety. I always just tell people that come here to testify, when we walk out of here, what are the one or two or three things that you want us to really be thinking about and to understand? Just hit us with those things.

Dr. Busch?

Dr. BUSCH. Thank you, sir, and thank you very much, Senator Stevens, Senator Hollings, and Senator Harkin, for the opportunity to address you gentlemen. My statement contains a few items of personal gratitude for: (a), being here and; (b), being part of the American system.

This year, I am president of the American Association for Cancer Research, which operates basically under Federal funding with the goal of conquest of cancer.

You have already said, Senator Harkin, many of the things that I would have said, except that I think that we should declare peace is the first thing I would like to say. We should declare peace. It is time, and I think that our Government has done a marvelous job in resurrecting Eastern Europe. Now I think we better attend to resurrecting the United States of America.

We are woefully deficient in crucial areas, and the first message that I would like to give is that the state of research in the United States is one of crisis, and the crisis has to do with cutting off young people who should be the Einsteins and the leaders of the future; that we have not provided adequate funding over a period of time for more senior investigators to continue in their research, and we are losing the enthusiasm of youth. We can't afford that. We are fully dependent on these 20- and 30-year-olds for our future as a nation.

The second item that I would like to comment upon is that science is really the only American frontier. We are frontiersmen. Our ancestors all came here for our frontier, and the only frontier that we have is growth and development intellectually and in terms of competitiveness. I might say, in connection with your statement, Senator Hollings, I spent 2 weeks in Japan 2 weeks ago visiting various universities and the Dikata Co., one of the great drug companies of Japan, and I am deeply impressed with the endeavor that they have made. A gentleman, Dr. Otsu, who took me around at the Dikata Co., gets to work every morning at 8 o'clock. He never gets home any day of the week before 10 o'clock. That man is symbolic of the intensity of Japanese endeavor.

Senator HOLLINGS. Sounds like a Senator. [Laughter.]

We make it home by 11:30 p.m. Go ahead.

Dr. BUSCH. Sir, I thank you for your comment, and I appreciate all of your many contributions.

So we need to have greater dedication and greater enthusiasm. I support the view that the NIH ought to have a thorough review at this time. I think that perhaps with an expenditure of almost $8 billion, and we hope you will add very substantially to that sum, that you ought to develop some kind of a board that would give you

some real insight as to how NIH operates. I know it is a small part of our total Federal budget, but I think that many years of service as a member of the executive committee of Eli Lilly & Co. taught me the virtue of the management of review and thoughtfulness about programs, operation and efficiency.

Perhaps some of the money ought to be spent to double people's salaries who are really productive rather than just paying across-the-board salaries. So I think perhaps a total review of the NIH would be of great value.

The last point that I would like to make is that perhaps the public should be aware of the immense opportunities for growth and development in the next 50 years. It is entirely possible that with a series of drugs, preventative and therapeutic, cancer can be resolved. I know that there is a certain angst about the fact that we haven't resolved the cancer problem, and you spoke about that, Senator Hollings, at our meeting a few weeks ago.

But we are just getting to the point now where molecular biology has provided us the tools where we can really construct drugs that are very novel, and I think that it would be worth your consideration to have a product development institute as part of our Government activities or support a product development institute, an institute that would take this vast body of knowledge that has accumulated and crunch it down to where we can really design effective drugs.

I will just take one moment to comment on my own experience. We have identified a very critical protein for cancer cell division. We have localized a target segment, an eight amino acid segment that is an optimal target segment, and then I went around to the NIH and various American drug companies and I said, "Fellows, can you fashion me a molecule, a drug, that can attack that particular cite?"

They said, "Well, we don't have the know-how. We don't know how to do this. We don't know how to start."

PREPARED STATEMENT

What we need is to transfer the information that we have obtained into the process of drug development. It is a big black box. When I spoke about this at the Dikata Co. in Japan, I got letters immediately after I got back to the company, "Tell us more; we want to hear more."

Fellows, we can't lose it all to Japan; we can't lose it all to Germany, and we can't lose it all to any other aggressive group. I thank you for listening.

[The statement follows:]

STATEMENT OF DR. HARRIS BUSCH

Gentlemen: I am deeply honored to have been asked to address this Senate Committee on behalf of American Science. I would like you to understand that I am indeed fortunate that my Grandparents came to this country 100 years ago and I have shared the inheritance of dedication to Scholarship and excellence that they brought with them from Germany and Russia.

I was born in Chicago in 1923 and I earned my M.D. at the University of Illinois and my Ph.D. at the University of Wisconsin. I served as a young Surgeon in the military and as a Medical Scientist on the faculties of Yale University, the Universi-

ty of Illinois and at Baylor College of Medicine in Houston, Texas, as Chairman of Pharmacology for the last 30 years.

It is currently my great honor to be President of the American Association for Cancer Research. This Association carries on the basic science and clinical research in Government, University and Industrial laboratories, which we hope will someday rid this world of the scourge of cancer.

The current state of research in this Nation is one of crisis. There is form but diminished substance; there is much research but too little "inspired" research. Much of our human and technological assets are being diverted from doing the job to bureaucracy and Institutional structure.

The greatest concern is the loss of "minds" from our Institutions because of frustration in obtaining resources with which to work and grow. Once we were the New York Yankees of the 1940's. Now, we are weakening our future by funding as low as 8 percent of new and worthy ideas and programs in major study sections. This has a devastating effect on recruitment of bright young college and high school students, who turn from inspiration to more lucrative and stable careers in business, law and clinical medicine.

We need a thorough objective review of the National Institutes of Health. Fiscal prudence and thoughtful leadership should welcome a status report for the present and for the year 2000. What are the problems, fiscal and programmatic, and how can these be addressed by the Institutes and by our vital extramural programs?

"Science is the only American Frontier", and we are rapidly becoming less competitive with other nations with greater dedication and greater enthusiasm. We cannot keep patting ourselves on the back about our great accomplishments of the past for that is the history of every decadent Nation. With only a mere decade to the next Century, this great body must attend the real future for our children and grandchildren.

In particular, I recommend consideration of major efforts in new Drug development based on the vast expansion of molecular biology. We need to develop a direct linkage between these technical advances which now provide specific drug targets and the chemistry that will provide us leadership in Industrial Drug Development. Our success will provide many jobs and much national revenues.

We have used over $3 trillion of our National Treasure in the correct and victorious efforts of the Cold War. That war is over. It is time to declare Peace. We need now to address that future for my 8 grandchildren and the heritage we wish them to share.

America is the greatest Nation with the most correct instincts and philosophy ever to be developed. Science and Medical Science are our National Number 1 priority. I am certain that you recognize with me that we need a vast infusion of resources for development, personnel and capitalization on new ideas for our Future.

Above all, it is crucial that this body leads in financial responsibility. We have a huge debt that mortgages future generations. Sooner or later we have to pay. We must act like a Great Nation now, 25 and 50 years hence.

STATEMENT OF DR. STEPHEN RYAN, PRESIDENT, DOHENY EYE INSTITUTE, PROFESSOR AND CHAIRMAN OF THE DEPARTMENT OF OPHTHALMOLOGY, UNIVERSITY OF SOUTHERN CALIFORNIA AT LOS ANGELES

Senator HOLLINGS. Very good. Dr. Ryan.

Dr. RYAN. Senator Harkin, Senator Hollings, Senator Stevens, staff, as a chairman of ophthalmology, I am pleased to address this committee on a matter of national concern, and one in particular, namely, blindness. As a direct result of your support for the National Eye Institute, sight truly is being saved and vision restored for thousands that were not helped 10 and 20 years ago.

Congress, with wisdom and foresight, has provided this financial support for vision research and the National Eye Institute, and this is guided by a series of 5-year plans that, in my opinion, really is strategic planning at its best.

A congressional resolution signed by President Bush designates these 10 years as the "Decade of the Brain." Anatomically, the eye is, in fact, an extension of the brain and the most easily accessible aspect of it. For those reasons, the visual system has always been

at the forefront of basic neuroscience. The visual system really serves as a premier model of the highest levels for information processing, control of movement and perception in the brain.

Vision research has also proven to be a very good investment. For example, the diabetic retinopathy study, which was a 9-year study funded by the National Eye Institute, cost $10.5 million. The treatment developed as a result of that study reduces the incidence of blindness from diabetic retinopathy by 60 percent with an annual savings of $51 million.

Another trial is retinopathy of prematurity, a disease which causes blindness in premature infants who must be treated with oxygen. This freezing treatment was found to be effective in 50 percent of these babies. Another way a health economist can calculate that, if you project that out over 65 years, the true savings in that is $960 million. Vision research is cost effective.

The humanitarian considerations in relation to the treatment of prevention of blindness, in my opinion, are second to none. On a purely economic basis, and as you pointed out, Senator Hollings, on the international front, it is essential, and support of biomedical research really is a very sound investment.

Overall, the NEI annual increase has averaged 3.4 percent per year for the last 4 years. This is below inflation, and it is less than half of what the NIH increase of 7 percent for those years has been. The NEI continues to emphasize investigator initiators, particularly these RO1 type of awards.

The recent series of budgets over the last 3 years has made it necessary for the NEI to cut back each grantee by 10 percent per year so as to stretch these limited dollars to fund as many grants as possible. Simply stated, going on this way, the research proposed by the investigators cannot be performed with these progressive cuts.

In addition, there has been no funds available for construction or renovation. There have been no new clinical trials in this year, 1990, or projected for the 1991 year. The NEI, in fact, has 10 important clinical trials which are conceived, drawn out with budgets all ready to go, but cannot be initiated for a lack of funding.

These clinical trials include, for instance, the role of treatment of CMV retinitis in AIDS patients. They also include a treatment for a clinical trial to look at the quality of life following treatment for glaucoma, and this study emphasizes cost effectiveness, which is built in in a prospective manner, measuring quality of life issues and outcomes related to the treatments that we routinely employ for millions of Americans today.

For reasons of time, I won't go into the other eight clinical trials, but they are all ready to go, but simply, they will not be started for lack of funds. The infrastructure and supportive vision research now and particularly in the future are being seriously weakened. Erosion of vision research is apparent to all of us, basic scientists and clinicians working in the field.

The NEI panels of experts who come together work hard to prioritize each of these proposals and each of these areas. So with this prioritized plan, the National Eye Institute can say to the public and to the Congress, we can accomplish this much in vision research with this much in the way of specific support.

National vision research has been immensely successful to date. It is, indeed, cost effective in terms of dollars, an improvement of the human condition and is poised on the brink of major accomplishments in each of its program areas.

If the budget of the NEI continues to decline in constant dollars as it has for the past 3 years, the impact on eye research will be far greater than what this relatively small reduction in dollars is.

PREPARED STATEMENT

Because rather, the key is, this will serve as a powerful disincentive to our best students, and it will give them the message that there is no real future in biomedical research.

I greatly appreciate the opportunity to deliver this testimony, and I will be pleased to entertain any questions.

Senator HOLLINGS. Very good. Thank you, Dr. Ryan.

[The statement follows:]

STATEMENT OF DR. STEPHEN RYAN

My name is Dr. Stephen Ryan. I am President of the Doheny Eye Institute and Professor and Chairman of the Department of Ophthalmology at the University of Southern California in Los Angeles. Thank you for the opportunity to address this Committee on a matter of national concern: the current status of research in this country and, in particular, blindness. As a direct result of the support this Committee has provided the National Eye Institute, sight is being saved and vision restored to thousands who once would have been hopelessly blind.

In the United States, one-third of all the 34 million visits to physicians' offices for medical care are made by citizens older than 65. More than 890,000 of these people are legally blind, with blindness in this age group increasing each year by 25,000. According to a Gallup survey, blindness was found to be the handicap or disability that Americans fear most and followed only AIDS, Cancer, and Alzheimer's as the "worst disease" in the minds of the American public. Visual disorders and blindness annually cost the nation more than $16 billion. Congress has, with wisdom and foresight, provided substantial financial support for vision research. Despite this support, more than ten million Americans have irreversible impairment from visual disorders.

The National Eye Institute has been guided by a series of five-year plans which represent the consensus of the best scientific minds from all across the country. I cannot emphasize too strongly that the vision research community is most pleased with, and supportive of, the National Eye Institute and the leadership of its Director and staff. Indeed, most of the senior vision scientists in this country readily contribute their time and efforts to it, for upon the success of the National Eye Institute depends the success of our research efforts. We are deeply concerned by the current restricted budgets for the NIH, in general, and the NEI, in particular in terms of their present effect, and even more alarmed regarding the future consequences. Before discussing the budget, I would like to make a few comments concerning the National Eye Institute and its programs.

The NEI was chartered by Congress to improve the prevention, diagnosis, and treatment of blinding eye diseases and other disorders of the visual system.

The National Eye Institute supports 70-80% of all vision research in the United States. Blindness can be measured in terms of both human suffering and its tremendous drain of the health resources of the nation.

Neuroscience and molecular biology and genetics are the fastest growing and most exciting areas of research at the National Institutes of Health. Further, among all the Institutes, the National Eye Institute is in the best position to immediately take advantage of numerous opportunities these fields have opened toward the conquest of disease.

The Intramural Program of the National Eye Institute supports complex collaborative projects involving research teams difficult or impossible to assemble in a university.

Clinical trials have proven to be remarkably effective in determining the efficacy of proposed treatments for blinding disorders. The first NEI multi-center clinical trial of laser treatment on diabetic retinopathy, the leading cause of new cases of blindness, cost some $10.5 million, whereas the annual saving is as much as $51 million if costs of lost productivity are included ($1.1 billion over 22 years). In addition to the direct economic savings, 82,000 vision years have been saved for American citizens over this time period. The most recently completed NEI-funded clinical trial relates to the retinopathy of prematurity, a disease that affects premature infants who must be given oxygen for them to survive. There are almost 27,000 low birth weight "preemies" born each year in this country. It is estimated that approximately 8,000 babies develop some retinal changes due to retinopathy of prematurity, which is characterized by an uncontrolled abnormal growth of blood vessels in their eyes. NEI-sponsored scientists in a clinical trial found that, by freezing abnormal retinal vessels, the disease can be halted and the risk of visual loss reduced by one half. The cost-effectiveness of this treatment is demonstrated by the fact that the NEI clinical trial cost some $9.6 million but the potential annual savings have been estimated conservatively as over $920 million over 65 years in social services, medical care, and lost earnings, to say nothing of the humanitarian consideration for the child and family.

The National Eye Institute has been remarkably effective in basic science in adapting the exciting developments in molecular biology, genetics,

and immunology to the opportunities in vision research. The gene responsible for retinoblastoma, the most common eye tumor in children, has been identified. We can now hope to devise more effective treatment and perhaps prevention of this deadly cancer of the eye. The breakthrough was achieved using the most modern techniques of molecular biology and molecular genetics and is having great ramifications, not only in ophthalmology but also in the whole battle against other types of cancer.

A congressional resolution signed by President Bush designates the last ten years of the 20th century as the Decade of the Brain. Since its establishment 20 years ago, the National Eye Institute has maintained a strong commitment to supporting neuroscience research. Anatomically, the eye is a highly accessible extension of the brain, and much of our ability to prevent and treat visual disorders depends upon a detailed knowledge of the structure and function of the entire visual system, including the eye, optic nerve, and visual pathways in the brain.

Furthermore, the visual system serves as the premier model of the highest levels of information processing, perception, and control of movement by the brain. In fact, research on the visual system has long been in the forefront of progress in understanding the general functioning of the nervous system, as a number of Nobel prizes awarded to vision scientists attests.

Today, nearly half of the NEI budget supports basic studies of how light falling upon the retina triggers a highly complex coordinated series of events that leads to visual perception and controlled movement of the eyes. Currently, among the research opportunities being actively exploited are studies of regeneration and transplantation of visual system tissue to foster recovery of function from ocular disease, trauma, and stroke. This work has important ramifications for all neurological disorders as well as rehabilitation of vision loss.

Thirty percent of genetic disorders affect the nervous system. To develop therapies for gene repair or gene replacement for people with inherited neural optic disorders, the NEI will continue to emphasize research on identifying and analyzing the genes that cause these conditions.

Important basic science advances in vision relate to our understanding of how messages are relayed among neurons, an important step in understanding

the growth of nerve processes and the development of treatment leading to regeneration in the nervous system and to transplantation of retinal cells that may someday offer hope of visual restoration for patients with macular degeneration and retinitis pigmentosa. There is so much to be done and we now have the scientific tools for great accomplishment, but lack the funds to proceed as we would like.

For the reasons of limitations of time and space in this report, I will focus on the clinical trials as they document the effect of the erosion of funding for the National Eye Institute, although the damage to basic research is of at least equal and probably even greater importance. The inability to develop our scientific base will adversely affect future clinical treatments.

The persistent erosion of NIH funding has impaired both basic science and clinical research programs of the NEI. Because of these limited budgets, we are not able to take advantage of a number of opportunities that are available in vision research. In investigating the total awards for the past three years, the NEI average annual increase is 3.4% less than half of the NIH 7.0%. In 1990 the NEI increase of 2.4% was the second lowest of any institute and below the NIH 6.0%. The higher award rate of NEI grants is not a result of the NEI having a disproportionate share of the NIH budget but rather of the NEI's long standing policy of making individual investigator-initiated research project grants its principal support mechanism. These so-called R01 and R29 grants keep the average grant costs at the NEI the lowest of any of the Institutes at the NIH. Unlike other institutes, the NEI does not support program projects or other large umbrella awards, such as multi-project center awards. For these reasons, one cannot readily make comparisons of the NEI award rate for ROIs to other Institutes. When adjusted to the NIH as a whole, the award rate for the NEI proves to be quite similar. The National Eye Institute staff has cut the current competing and non-competing grants by 9%, 11%, and 10.3% in 1989, 1990, and 1991 so as to stretch the actual number of grant awards. These cuts have severely restricted the ability of vision scientists to perform the research which they have proposed. Within the budget limitations, the NEI has maintained an award rate of 41.6% for 1990 and 37.7% for 1991. In summary, by emphasizing R01 and R29 grants the NEI is able

to keep its grant costs low and therefore the NEI is able to fund additional grants.

The NEI appropriation has increased by 3.8%, 4.1%, and 2.4% for the years 1988, 1989, and 1990. At the same time, overall NIH has increased by 7.8%, 7.2%, and 6.0%. For these three years, the overall NEI average of 3.4% is less than half of the NIH 7.0%. We should note that there have been no new awards for construction or renovation. A private organization, Research to Prevent Blindness, Inc., surveyed more than 80 departments of ophthalmology in this country and determined the national need for construction for laboratory space to be more than 1,000,000 square feet at a cost of $300 million to keep pace with modern technology available to vision research nationally. This critical need is not being met.

There have been no new clinical trials in 1990 or in 1991. Ten important clinical trials and epidemiologic studies have been designed, including budgets, and are ready to go but cannot be initiated for lack of funding. I will cite only three examples that cannot be initiated for a lack of funds. One is the expanded studies of the treatment of CMV retinitis in AIDS. With the devastating effects of AIDS, we should emphasize that more than 50% of these patients have eye complications. CMV retinitis is a viral infection of the retina that leads to blindness in these immuno-compromised patients. The desire to maintain vision for a person with a terminal illness is a compelling humanitarian reason for such a trial and study.

Another important clinical trial awaiting funds would evaluate the quality of life following glaucoma treatment. The science and technology of measuring outcomes and evaluating the impact of treatment on all aspects of the quality of life are of vital importance. In ophthalmology, we are applying these scientific measures and approaches in these difficult and common clinical problems, so as to better understand the cost-effectiveness and the quality of life issues related to treatments that we prescribe for millions of Americans.

A third major trial is the treatment of congenital esotropia or "crossed eyes" in children. Eye surgeons have debated for a long time the contradictory opinions as to the proper type and timing of surgery or intervention to help children with esotropia or "crossed eyes." There is now

the hope of finally resolving this debate which has raged for years. This study will directly affect the lives of tens of thousands of children across the country.

The training programs in vision research have suffered greatly as a result of these severe budget constraints. There is a demonstrable need for more clinical investigators, which does relate to the level of stipends for individuals to pursue clinical research. There is the need for more basic scientists as it relates to molecular biology, immunology, and molecular genetics. The infrastructure and support for vision research in the future are being seriously weakened by the effects of the budgetary reductions of today.

The panels of experts in vision research convened by the National Advisory Eye Council and committees work hard to prioritize and update the identification of those areas of most critical importance to vision research. We have not identified just a dream, but, rather, are pointing out the very real opportunities for concrete progress in prevention vision and treatment of blindness. With this plan in hand, we can, in effect, say to Congress and the public, "We can accomplish this much in vision research if you are willing to invest this specific amount of money."

I have attempted to demonstrate the breadth and importance of National Eye Institute-supported research with a focus on clinical trials. It is apparent that our research program represents a national consensus, has been immensely successful to date, is cost-effective in terms of dollars and improvement of the human condition, and is poised on the brink of major accomplishments in each of its program areas.

We recognize the tremendous challenge for Congress related to the budget and the many competing demands for support and limited revenues. We believe that vision research and support of the National Eye Institute has proven to be cost-effective and of enormous benefit to the American public. The research plan for the National Eye Institute represents a national consensus of vision scientists. This process is again underway to create the next five-year plan, which will guide the National Eye Institute in its granting on a priority basis. We are poised on the brink of several opportunities to make major new accomplishments in each of the program areas of the National Eye Institute.

If the budget of the NEI continues to decline in constant dollars as it has for the past three years, the impact on the eye research community will be far greater than the small reduction in purchasing power that smaller budgets will allow. Rather, it will serve as a powerful disincentive to our best students and will give them the message that there is no real future in biomedical research.

I greatly appreciate the opportunity to deliver this Testimony. I will be pleased to entertain any questions about any aspects of the current status of research. Thank you.

NATIONAL INSTITUTES OF HEALTH

National Eye Institute

Appropriations History

Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation	NEI Annual % Increase	NIH Annual % Increase
1987	$179,201,000	$219,091,000	$214,080,000	$216,637,000		
1988	184,829,000	234,382,000	231,529,000	224,947,000	3.8%	7.8%
1989	229,021,000	223,288,000	229,271,000	234,218,000	4.1%	7.2%
1990	233,777,000	240,636,000	241,774,000	239,889,000	2.4%	6.0%
				OVERALL AVERAGE	3.4%	7.0%

STATEMENT OF DR. WILLA A. HSUEH, IMMEDIATE PAST PRESIDENT, AMERICAN FEDERATION FOR CLINICAL RESEARCH, PROFESSOR OF MEDICINE, UNIVERSITY OF SOUTHERN CALIFORNIA SCHOOL OF MEDICINE

Senator HOLLINGS. Dr. Hseuh, did I pronounce that correctly?

Dr. HSEUH. Hseuh.

Senator HOLLINGS. Hseuh? That easier for me.

Dr. HSUEH. I know you all like California. There are three of us. California LAUSC stands for Los Angeles County University of Southern California. I am professor of medicine at the University of Southern California and immediate past president of the American Federation of Clinical Research, which is the Nation's largest organization of medical investigators.

I am pleased to be here today to have this opportunity to talk to the subcommittee about an issue of very special importance to the American Federation for Clinical Research, and that is something you have all brought up this morning, the declining number of physicians pursuing careers in research.

It is very sad and frustrating to see talented physicians who may have made outstanding contributions to biomedical research, to see their interest diverted because of the risks and insecurities of a career in science, and these insecurities may outweight the benefits.

The physician scientist is a key player in the biomedical research enterprise. He or she alone has the perspective and the expertise to

bring clinical insights to basic research and conversely, to practically apply the results of scientific knowledge to the care of patients.

The dramatic growth in the application rate for NIH research project grants in the past 10 years has not been physicians, but really, nonphysician scientists. Overall, the proportion of physicians primarily engaged in research has fallen sharply in the past 20 years, and this trend is expected to continue.

Why have we seen such a decline? Well, it is increasingly difficult as physicians to obtain research support. Because the NIH award rate has fallen off so badly and the number of physicians applying has not increased, physicians as a group stand increasingly poor chances of obtaining NIH funding. Even those who succeed in obtaining an NIH grant are forced to cut corners because of the so-called downward negotiations.

I myself have had to cancel studies in high blood pressure research because of a 13-percent cut in my own grant. We may be receiving a center grant, which the downward negotiations are predicted to be 25 percent.

Basic biomedical research has changed. Prior to the 1970's, medical research was primarily the responsibility of physicians, some with little formal training in science. Today, the Ph.D.'s or M.D.'s must have extensive basic science training and experience to compete successfully for NIH RO1 grants. Therefore, physicians must spend additional time beyond their medical training years to master the complexities of modern biomedical research.

Another problem is that those physicians interested in pursuing patient-oriented research have recently been confronted with the new challenge, the growing unwillingness of third-party ensurers to cover the cost of care for patients involved in research protocols. Medicare policy already precludes payment for investigational therapies, even if they are the best available treatment.

Another problem: Often the pressures of high medical school debts lead physicians who might otherwise consider research into other career paths. Physicians who complete their subspecialty training are not anxious to pursue a research fellowship which will provide them with a smaller stipend than they even receive as residents.

Some of the recommendations of the AFCR include: One, an increase in training support to allow NIH to offer post-doctoral training stipends that are at least as attractive as residents' salaries and to raise stipends annually;

Two, to increase the number of career development awards, and these are for the young physician scientists after their fellowship training to a minimum salary level of $50,000;

Three, the establishment of a program to repay or forgive portions of medical school loans of physicians who made a long-term commitment to research training and career development;

Four, an overall increase in NIH funding to allow greater numbers of meritorious research projects to be fully supported;

And five, let's modify Medicare payment policies that discourage patient participation in clinical trials or other forms of clinical investigation.

I realize that these solutions we offer cost money. We believe that the NIH budget requires and merits steady budget increases of 20 to 25 percent annually over the next several years. Specifically, for the fiscal year 1991, we endorse the recommendation of the ad hoc group for medical research to an NIH budget of $9.2 billion. This amount may seem large when one realizes that the military research program receives $40 billion a year, over four times what we are requesting for NIH.

The 22-percent increase may seem fiscally impossible until one considers the 32-percent increase for NASA research efforts and the 26-percent growth in transportation research and development proposed by President Bush. If we can afford to strengthen these programs, certainly, we can afford to strengthen the NIH budget.

We are confident that you and the members of this subcommittee would like to substantially increase Federal support for biomedical research, so we, in our efforts, are rolling up our sleeves and expanding our efforts to convince your colleagues to support a much larger investment in the NIH effort.

I brought with me several hand-outs which I would just like to give you, which is a chart. I have your names on them.

These include a press release distributed on Monday contrasting the Bush research and development request with the results of two recent AFCR commission polls indicating that the American public and Congress overwhelmingly support funding increases for health research ahead of budget research for weapons, energy or space-related research and development.

We also put in an advertisement that appeared in the Roll Call suggesting that medical research should be made a Federal priority, and this is also included in that briefing package. This document that you have is presented in the format of a patient file. Medical research is the patient, and President Bush and Members of Congress are the attending physicians.

This document has been distributed to all of the media and will be sent to every Member of Congress this spring. We hope it presents our case in a sufficient fashion to attract greater support for the need for biomedical research.

Mr. Chairman, I would like to close on a personal note. I will continue to fight for a career in biomedical research, and I will continue to strive to convince young, talented physicians that a career in research can be a wonderful and challenging position. However, I can't promise you that I will encourage my two young sons, ages 3 and 11, to follow in my footsteps when their turn comes. Certainly, I will not do so if our Government remains more committed to exploring space and and developing weapons than it is to curing disease.

PREPARED STATEMENT

On behalf of the American Federation for Clinical Research, I thank the subcommittee for allowing me to express the problems of the physician in research and to consider taking these problems seriously and to looking for cures for these problems. I ask this subcommittee to respond to our request and to the wishes of the over-

whelming majority of American taxpayers by making biomedical research a national priority.

Thank you.

Senator HOLLINGS. Thank you, Dr. Hsueh.

[The statement follows:]

STATEMENT OF DR. WILLA A. HSUEH

My name is Willa Hsueh and I am a professor of medicine at the University of Southern California School of Medicine. My research efforts focus on clinical and basic aspects of high blood pressure. I am the immediate-past president of the American Federation for Clinical Research (AFCR), the nation's largest organization of medical investigators. The AFCR is comprised of nearly 13,000 physician and non-physician scientists who are engaged in virtually every area of medical research. The programs of the National Institutes of Health (NIH) are of crucial importance to AFCR members as many of us rely heavily on funding from the NIH extramural program.

Mr. Chairman, I am extremely pleased to have this opportunity to talk to the members of this Subcommittee about the challenges confronting medical research in the 1990's. I will focus my remarks on an issue of special importance to the AFCR: the declining numbers of physicians pursuing careers in research. In recent years, it has been sad and frustrating for me to see talented physicians who might have made outstanding contributions to biomedical research diverted because the risks and insecurities of a career in science outweigh the benefits. I have watched colleagues who were well-established contributors to the research in their fields "close up shop" because their very high priority scores fell below the NIH payline and they could not secure funding from other sources for their basic studies. In addition, I have seen the devastating impact of inadequate funding opportunites on young scientists trying to decide whether to pursue careers in research and medicine.

The decline in basic research opportunities for physicians is quite troubling because the physician-scientist is a key player in the biomedical research enterprise. He/she alone has the perspective and expertise to: 1) identify crucial clinical

elements that contribute to the cause and functional manifestation of disease, 2) develop a logical approach to the disease based on a rational combination of medical and/or surgical interventions, and 3) practically apply the results of scientific knowledge at the bedside to test new therapies and diagnostic techniques. The physician-scientist is the foundation that closes the gap between bench research and the sick human being.

While the total number of active physicians in the U.S. increased from 300 to almost 550 thousand between 1968 and 1987, the proportion of physicians primarily engaged in research has dropped from 5.2 to 3.1%. A recent report by the National Academy of Sciences regarding biomedical and behavioral research personnel needs suggests that this trend is apt to continue. The report stated the following:

> There is no reason to assume that the number of M.D.'s available for clinical investigation will increase because of an oversupply of physicians who find patient care less satisfying... nor is there any basis to assume a reduction in the research attrition rate.

In other words, more physicians does not mean more physician-scientists. In fact, most of the growth in the application rate for NIH research project grants has been among non-physician scientists. As Attachment 1 shows, there has been almost no increase in the number of M.D.'s applying for NIH grant support.

Why has the percentage of physicians opting for research careers declined? There are many contributing factors, but several are particularly noteworthy:

- It is increasingly difficult for physicians to obtain research support. Because the NIH award rate has fallen and the number of physicians applying has not increased, physician applicants as a group stand increasingly poor chances of obtaining NIH funding. Even those who succeed in obtaining an NIH grant are forced to cut corners as a result of across-the-board cuts, euphemistically known as "downward negotiations." For

example, my own grant was reduced by 13% below the study-section-approved level. As a result, I am unable to hire a technician and have had to cancel some planned studies that might have yielded important results. Downward negotiations may enable NIH to fund more grants, but I can attest to the fact that they mean less research and a lot more frustration.

- Medical school faculty members have less time available to do research. Their patient care responsibilities have grown dramatically as medical schools rely increasingly on professional service fees as a source of revenue. In 1971, professional service income represented 12% of total U.S. medical school income. By 1987, 38% of medical school revenue was from patient care reimbursement.
- Basic biomedical research has changed. Prior to the 1970's, medical research was primarily the responsibility of physicians, even those with little formal science training. The science taught in medical schools was often the basis of the research. Today, only Ph.D.s or M.D.s with extensive basic science training and experience can compete successfully for NIH R01 grants. Physicians must spend additional time beyond their medical school and residency training years to master the complexities of modern biomedical research. In fact, residency training offers almost no opportunity for research experience and in effect temporarily disconnects physicians from scientific pursuits. It is often difficult for those who developed an interest in science during medical school to re-enter today's fast-moving biomedical research laboratories after an absence of three years or more.
- Often, the pressures of large medical school debts lead physicians who might otherwise consider research into other career paths. In the short term, physicians completing their specialty training are not anxious to pursue a research fellowship that will provide them a smaller stipend than they received as residents. In the long term, physicians can

anticipate more lucrative career opportunities outside of scientific laboratories.

- Those physicians interested in pursuing clinical research involving patients have recently been confronted with a new challenge: the increasing unwillingness of third-party insurers to cover the costs of care for patients involved in research protocols. Medicare policy already precludes payment for investigational therapies even if they are the best available treatment. A 1988 report by the Institute of Medicine stated that medical insurers can be expected to "move vigorously to cut costs by denying payments for all services where any investigational protocol is involved" and further that "third party payers have been unresponsive to arguments that it is in their long term interests to fund clinical trials and related clinical investigation." The combination of an extremely limited NIH budget for clinical trials and an insurance industry that refuses to pay for the care of research patients makes a career in patient-oriented investigation a tenuous endeavor at best.

The AFCR would like to offer several specific suggestions to address these problems:

- NIH training programs need to be strengthened. Since 1971, the percentage of the NIH research dollar devoted to training has declined from 18 to 5%. Increased support for training would enable the NIH to offer postdoctoral trainee stipends that are at least as attractive as resident salaries and to increase stipends annually.
- The number of career development awards for intensive research training of physician-scientists should be expanded, and the salaries for these awards should be increased to $50,000 per year.
- A program should be established to repay or forgive portions of the medical school loans of physicians who make a long-term commitment to a program of research training and career development.

- o NIH funding should be increased to allow greater numbers of meritorious research projects to be fully supported.
- o Congress should mandate modification of Medicare payment policies that discourage patient participation in clinical trials or other clinical investigation. Last year, the AFCR submitted comments to the Health Care Financing Administration along these lines (see Attachment 2).

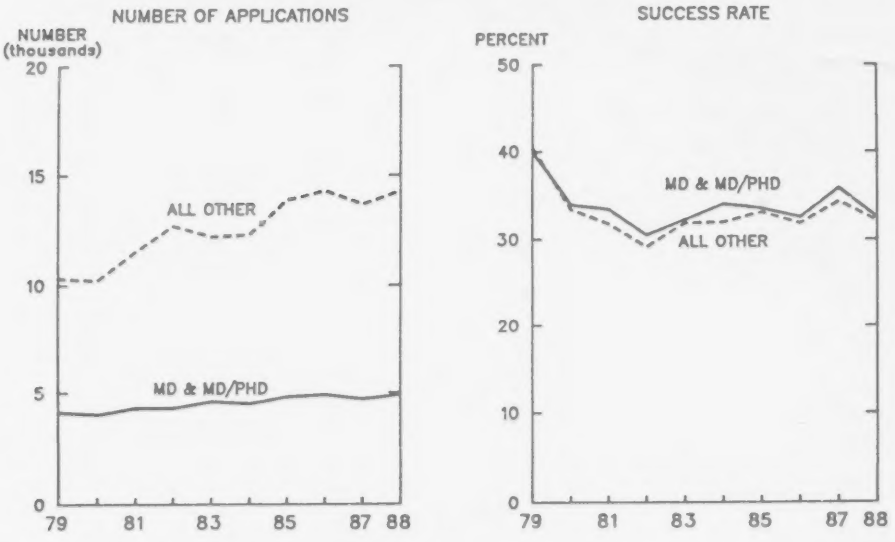
Clearly, the solutions we offer cost money. The AFCR believes that the NIH budget requires and merits steady budget increases of 20 to 25% annually over the next several years. Specifically for FY 1991, we endorse the recommendation of the Ad Hoc Group for Medical Research Funding for an NIH budget of $9.237 billion. The amount may seem large until one realizes that the military research program receives almost $40 billion per year, over four times what we are requesting for NIH. The 22% increase may seem fiscally impossible until one considers the 32% increase for NASA research efforts and the 26% growth in transportation R&D proposed by President Bush. If our government can afford to strengthen these programs, it can certainly afford a $9 billion NIH budget.

The AFCR believes that you and the members of this Subcommittee would like to substantially increase Federal support for biomedical research. We will do what we can to convince your colleagues to support a much larger investment in the NIH effort. I sincerely believe that to do otherwise will mean missed opportunities to rapidly uncover the answers to a host of diseases and disorders that are weakening our people and bankrupting our nation. I know that to do otherwise will mean the loss of a generation of physician-scientists. Mr. Chairman, at the age of 41, I will continue to fight for a career in biomedical research. I will not be discouraged from trying to convince young, talented physicians that a career in research can be a wonderful and challenging experience. However, I cannot promise you today that I will

encourage my sons, now aged 3 and 11, to follow in my footsteps when their turn comes. Certainly, I will not do so if our government remains more committed to exploring space and developing weapons than it is to curing disease. On behalf of the American Federation for Clinical Research, I ask this Subcommittee to make biomedical research a national priority.

ATTACHMENT 1

NUMBER OF APPLICATIONS AND SUCCESS RATES
FOR NIH COMPETING RESEARCH PROJECT GRANT APPLICATIONS
MD AND MD/PHD DEGREES COMPARED TO ALL OTHERS, FISCAL YEARS 1979–1988



SOURCE: NIH, DRG, INFORMATION SYSTEMS BRANCH

8801-E45

ATTACHMENT 2

LETTER FROM THE AMERICAN FEDERATION FOR CLINICAL RESEARCH

Room 309-G
Hubert H. Humphrey Building
200 Independence Avenue, S.W.
Washington, DC 20201

March 31, 1989

Re: BERC-432-P

Dear Sir or Madam:

I am writing on behalf of the American Federation for Clinical Research (AFCR). The AFCR is comprised of more than 13,000 physician and non-physician scientists who are engaged in virtually every area of medical research. We would appreciate your consideration of our views regarding the proposed rule published in the January 30, 1989 Federal Register: "Medicare Program: Criteria and Procedures for Making Medical Services Coverage Decisions that

Relate to Health Care Technology." Our comments will focus on two aspects of the proposed rule: 1) provision for limited coverage, and 2) coverage for "experimental" services.

Provision for Limited Coverage

The AFCR agrees that in certain cases, HCFA should "provide for coverage but impose such limitations as facility or patient selection criteria" and that the agency should have the option to "revise a coverage policy based on subsequent data collection." However, the proposed rule seems to suggest that such policies would apply only with regard to the evaluation of "breakthrough" procedures. We would suggest that HCFA delineate specific criteria for limited coverage decisions and for the revision of coverage policy with the intention of applying these standards to any treatment or procedure. Coverage determinations should not be viewed as irreversible, "all or nothing" propositions. HCFA should have the option to revise coverage policy and should have the flexibility to pay for a service in circumstances where it is known to be effective and deny coverage in circumstances where it is not.

Coverage for Experimental Services

At the request of the National Institutes of Health, the Institute of Medicine (IOM) of the National Academy of Sciences recently conducted a study to assess the availability of appropriate resources for patient-oriented research. The first recommendation in the 1988 report of that study is as follows:

> Third party payers (government and non-government) should pay the necessary and appropriate patient care costs for beneficiaries enrolled in approved clinical investigation protocols. This requires a clarification in current Medicare regulations involving definitions of medically necessary care.

With regard to "experimental or investigational considerations," the proposed rule states that:

> A service that is furnished for research purposes in accordance with predetermined rules is considered experimental or investigational and is not covered by Medicare.

We strongly urge that a statement be added to this section of the final rule to implement the policy recommended by the IOM. Specifically, it should be explicitly stated that Medicare will cover the necessary and appropriate patient care costs for beneficiaries who are participating in research studies. It is inappropriate for Medicare to deny payment for patient costs that would be incurred in any case simply because a patient happens to be involved in a research protocol.

In addition, the AFCR believes that the final rule should delineate criteria under which HCFA would have the flexibility to provide coverage for some experimental treatments. In cases where no other treatment has been proven safe, medically effective, and cost-effective, limited coverage should be provided for experimental treatments that are known to be safe and potentially effective.

Selected providers could be designated to receive payment for an experimental service under specified circumstances in exchange for data regarding the effectiveness of the new procedure. In this way, HCFA could use the coverage process to assist in identifying effective--and ineffective--treatments. In addition, this limited

coverage would ameliorate some of the problems outlined in an article published in the July 7, 1988 issue of the New England Journal of Medicine:

> By refusing to cover the costs of investigational therapy, third-party carriers are in fact making decisions about the care of patients. In practice, they are equating investigational treatment with no treatment. If the health insurance industry does not cover investigational therapy, only affluent patients will have access to promising treatments...

A copy of the complete article is provided for your information.

Conclusion

In summary, the AFCR supports efforts to refine the criteria for Medicare coverage of reasonable and necessary services. However, in our view, the final rule should include additional provisions to:

- allow for limited coverage of both traditional and "breakthrough" procedures,
- assure coverage for the necessary and appropriate patient care costs for Medicare patients involved in research, and
- provide HCFA with flexibility to support some experimental procedures.

We appreciate your consideration of the views of the AFCR. If there are questions regarding our comments, please call Ms. Lynn Morrison in our Washington Office at 202-293-0103.

Sincerely,

Willa A Hsueh

Willa A. Hsueh, M.D.
President

ATTACHMENT 3

[From the New England Journal of Medicine, July 7, 1988]

SOUNDING BOARD

THE CRISIS IN CLINICAL CANCER RESEARCH

Third-Party Insurance and Investigational Therapy

CLINICAL cancer research is in jeopardy. Current budgetary constraints on federal support for biomedical research, the escalating costs of health care delivery, and the recent refusal of some third-party payers to support the costs of patient care as part of research trials threaten to compromise clinical investigations that might lead to progress in the treatment of cancer.

This situation has arisen despite advances over the past four decades that have led to curative therapy for childhood leukemia, Hodgkin's disease, non-Hodgkin's lymphoma, cancer of the testis, and many solid tumors in children. Clinical research has also substantially reduced mortality among premenopausal women with breast cancer and has improved the palliative treatment of other common neoplasms. More than 30 effective antineoplastic agents have been identified through clinical trials. The most recent agents to become commercially available, cisplatin and etoposide, have helped cure the majority of young men with metastatic cancer of the testis.[1]

A full appreciation of the problems of funding for patient care in clinical research requires an understanding of both the process whereby promising new treatment approaches are evaluated and the patients who participate in these studies. Developing a new, effective therapy requires an orderly progression of investigations. Phase I studies identify the maximal safe dose of a new agent, whether it is a new drug, an antibody, an immunotoxin, or a biologic-response modifier. These studies involve 15 to 25 patients and are conducted almost exclusively in specialized research centers, where coordinated clinical, pharmacologic, immunologic, and other studies are performed. Phase II studies evaluate the therapeutic effects of the new agent at the dose schedule identified in the phase I trial and require approximately 20 patients with a given type of cancer. Thus, the evaluation of a drug's effects on five representative types of tumors requires approximately 100 patients. Hospitalization is less often required for phase II than for phase I studies. Phase III studies are randomized clinical trials that compare a standard therapy with a new treatment. Once three or four sufficiently active single drugs have been identified, it has been possible to cure certain diseases by devising effective combination therapies. Examples include mechlorethamine, vincristine, procarbazine, and prednisone (MOPP)[2] or doxorubicin, bleomycin, vinblastine, and dacarbazine (ABVD)[3] for Hodgkin's disease, and vinblastine, bleomycin, and cisplatin (VBP)[4] for cancer of the testis. With the use of optimal combination chemotherapy early in the disease (e.g., with adjuvant chemotherapy for breast cancer), somewhat less sensitive tumors may also be cured.[1] Although these are examples of strategies for clinical trials of chemotherapy, the same principles also apply to trials of other systemic treatments, such as immunologic, biologic, and hormonal interventions, to surgical trials of organ preservation (such as the preservation of the breast, limb, and bladder), and to trials of developing techniques and procedures such as bone marrow transplantation. That the majority of advanced cancers remain incurable underscores the importance of safeguarding the mechanisms for performing clinical research as new ideas and concepts emerge.

It has proved difficult, if not impossible, to estimate accurately the actual costs of investigational patient care. Only a minority of the approximately 500,000 persons who die of cancer every year in the United States ever participate in clinical trials. Most participating patients are treated as part of phase III randomized trials, in which standard therapy is compared with promising new treatments. Because phase III trials include standard therapy, the costs of patient care are frequently covered by third-party payers. Fewer patients participate in phase I and II trials, although these trials are absolutely essential, since all phase III trials are based on them. Phase I and II studies are particularly vulnerable in the current economic climate, in which the reduction of the costs of medical care is emphasized.

Who are the patients who participate in clinical cancer research? They include the majority of persons with advanced cancer, for which no known cure is available. When informed of the gravity of their disease, many such patients ask for and even insist on investigational therapy. Many will refuse a recommendation that no therapy be undertaken, even if the physician indicates that this is a reasonable and humane course of action. Increasingly, health insurance companies have refused to cover investigational therapy, which is defined as treatment with any drug not approved by the Food and Drug Administration or treatment that uses approved drugs in doses or schedules that are not approved. Health care insurers are under great financial pressure and are understandably committed to reducing the costs of health care. Because this policy applies broadly to other areas of medical research, the issues in cancer therapy also arise in other medical disciplines.

How should the costs of clinical research be borne? One approach would have patients cover these costs themselves. This would have the effect of guaranteeing that new, experimental therapies would be available only to the affluent members of society.[5,6] Furthermore, patients who served as controls in comparative studies would presumably not pay for treatment.

A second approach would include the costs of patient care in research grants. The American people, through Congress and the National Cancer Institute,

have consistently assigned a high priority to clinical cancer research. In the past the National Institutes of Health provided important financial support for the care of patients in selected clinical research trials through grants to individual projects or clinical centers. Recently, however, funding for the costs of patient care has largely been deleted from research budgets, and these costs have been assumed by the patients, their health insurers, or both. Current research grants generally cover the costs of collecting data, histologic review of slides, and laboratory tests not otherwise required for patient care. The research cost per patient for a phase I or II trial is generally in the range of $1,000 to $2,000. If hospital admission is required for the research treatment, including patient care in research grants would require an enormous increase in funding, creating unacceptable financial pressure on the budget of the National Institutes of Health, which is already constrained. Furthermore, patients with advanced cancer require hospitalization for a variety of complications that are often unrelated to the administration of investigational therapy. These costs are properly paid for by the patients' insurance companies. Budgetary constraints currently imposed on federal support for biomedical research almost certainly preclude grant support for the costs of providing patients with investigational treatments.

A third possibility is that the pharmaceutical industry could support the costs of patient care in clinical research. By the time new pharmacologic agents enter clinical trials, the pharmaceutical firms have already invested substantially in drug development. They frequently provide drugs at no cost and, in some cases, cover the costs of laboratory tests associated with clinical trials. Requiring that drug companies cover all expenses incurred during hospitalization would be a major financial disincentive to investment in this industry and would be unfair for the same reasons that funding the costs of patient care through grants is inappropriate: patients with advanced metastatic cancer require hospitalization for a variety of complications, which may be unrelated to the investigational therapy. Pharmaceutical firms should not be responsible for the costs of treating the complications of the underlying cancer.

Historically, the hospital expenses of patients participating in phase I and II studies have been paid for by the health insurance companies from which they and their employers have purchased insurance. Is this practice appropriate, and should it continue at a time when health care costs are rising? The answer depends on the definition of the best available medical treatment. In the absence of a research trial, many patients with advanced cancer would be treated with FDA-approved therapies despite their lack of demonstrated benefit. Standard therapy for metastatic colorectal or non-small-cell lung cancers, for example, may produce partial regression of tumors in a minority of patients at some cost in toxicity, but with no improvement in survival. Such marginal treatments are routinely administered, and their costs are covered by third-party payers. The limited effectiveness of such standard therapy emphasizes the justification for scientifically and ethically sound trials of novel treatments, which, at the least, provide hope for the patient and his or her family. Most patients assume that they are covered by health insurance for the costs of an investigational therapy if no effective standard therapy exists for a lethal disease. They are surprised and frequently angry to discover that the insurer will not cover these costs.

Failure to cover the costs of patient care in trials of promising therapies poses an ethical dilemma, since the available curative treatments for childhood and adult cancers were all initially considered investigational. The patients who participated in those studies were the first to benefit from the treatments. In the appropriate clinical setting, investigational treatment should be equated with "state-of-the-art" care. Thus, the participation of patients with advanced, incurable cancers in therapeutic trials — assuming that the clinical studies are scientifically and ethically sound — is the best available form of medical care. Certainly, the "best" patient care should be covered by third-party payers. The costs of this type of care are ultimately borne by the present and future consumers of health care, who are the ultimate beneficiaries of any medical advances resulting from the clinical trial. Investigational treatment may increase medical costs in the short run. When these treatments lead to curative therapy, however, the costs of an illness to society, in terms of both medical costs and lost productivity, will decrease. In the long run, therefore, clinical investigation is cost effective.

A related issue is the treatment of a patient with an experimental therapy as a "compassionate exemption." In this case, the drug — usually one that has some efficacy, on the evidence of clinical studies already undertaken, but that is not yet approved by the FDA — is supplied to the physician by the National Cancer Institute or the pharmaceutical company for a specific patient with a minimum of paperwork. In this case, the intent is clearly the treatment of the patient, with no additional requirement to collect data. The cost of such a treatment should be reimbursable, although in this case society does not obtain the benefit of additional research information.

The assumption of the cost of patient care in clinical research by third-party payers requires rigorous safeguards of the scientific foundation and design of a study, its potential importance, and its ethical basis. Third-party insurers should be brought into the process by which investigational treatments are coordinated by the National Cancer Institute and regulated by the FDA. Implicit in this suggestion is adherence to standards to ensure that only studies with scientific value and potential social importance will be ap-

proved for coverage. In addition, Congress should do its part by requiring that Medicare cover the costs of participation in clinical trials. Since the government is also one of the largest employers in the country, Congress should also insist that government employees' participation in clinical trials be covered. For Medicare patients, at least, whether funds are allotted through Medicare or through research budgets, the cost would then be paid by tax dollars.

The current system of refusing to pay the costs of hospitalization when patients receive investigational therapy is expensive to monitor, unfair to many patients, and arbitrary in distinguishing between the best available patient care and investigative treatment. By refusing to cover the costs of investigational therapy, third-party carriers are in fact making decisions about the medical care of patients. In practice, they are equating investigational treatment with no treatment. If the health insurance industry does not cover investigational therapy, only affluent patients will have access to promising treatments, and both progress in clinical cancer research and, ultimately, treatment for all will be seriously compromised.

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STATEMENT OF DR. DAVID KORN, VICE PRESIDENT AND DEAN, STANFORD UNIVERSITY SCHOOL OF MEDICINE AND CHAIRMAN, NATIONAL CANCER ADVISORY BOARD

Senator HOLLINGS. Dr. Korn.

Dr. KORN. Good morning. My name is David Korn. In addition to being the dean of Stanford Medical School, I have been serving for the last 6 years as chairman of the National Cancer Advisory Board.

I would like to share some generic thoughts with you rather than specific institutes or disease-oriented thoughts. First, I think we should keep in mind that in the United States, unlike any other country in the world, the vast majority of basic biomedical research is taking place in our Nation's universities where the discovery of new knowledge and education of the next generation of scientists takes place in an intermingled, confluent process.

In a world where much of our Nation's output is overtaken by foreign competitors, I would I maintain that the U.S. system of research and research education remains the goal of standard. While we have a preeminent biomedical research system, I think there are some very disturbing trends that threaten its long-term health and vitality. I think both Congress and the research community need to come to grips with these.

First, grants. Despite the real growth in the NIH budget over the last decade, we are facing two major problems with respect to the funding the NIH-supported biomedical research. There is an imbalance between the availability of resources and the demand for them, and that means that a good deal of superb, extraordinarily promising research is simply not being funded.

Second, the research that is being funded is often being supported at reduced levels that threaten its integrity. I know from my own almost two decades of experience as a principal investigator that the investigator submits a lean and thoughtful budget in a research proposal; that the assessment of those proposals by NIH study sections is hardnosed, and almost invariably, the amount of funds requested is reduced by the study center.

In the present climate, however, because of a conscious policy of trying to set a numerical funding target of numbers of awards, the NIH has now developed, almost as new routine, what is called euphemistically downward negotiation, a process that means that NIH will chop an additional 10, 15, even 20 percent from the amount that goes through the merit evaluation. This is a unique form of double jeopardy, a thoughtfully constructed budget first reviewed by knowledgeable scientific reviewers, and then arbitrarily slashed by the funding agency.

Second, during the decade of the eighties, training grants have been chronically and embarrassingly underfunded, and I hope that Congress will keep in mind the demography of the working population of research scientists and the wounding retirement problem we face as we approach the end of this century.

It is critically important to the sustenance of our biomedical research enterprise that we deal with the need for training, but training is also not a numbered stamp. There is a climate factor, as others have said this morning. American youth have an enormous diversity of career options available to them, and many of them are much easier and much more lucrative than pursuing academic careers in research or in education.

A forbidding and hostile climate engendered by the underfunding of our investment in biomedical research does not attract the best and the brightest careers in biology and medicine.

Finally, facilities. Most of our research facilities were built 25, 30, or 40 years ago, and the combination of scientific advancements, growth and technological complexity and the enormous growth in regulatory complexity have led to remarkable rates of obsolescence. Many of our facilities simply cannot accommodate biomedical research efficiently or safely. While universities are certainly aggressive at fundraising, and all alumni will testify to that, we just can't meet the enormous accumulation of pent-up facilities used through those avenues.

So in summary, if I could leave you with a thought, I would like to ask you to believe that we must treat the Federal support of biomedical research as an investment. It is an investment in the future; it is an investment in our children, and as an investment, we must make policy and budgeting decisions that take into account long-term consequences.

Nature is awfully sophisticated, terribly clever and terribly complicated. Unraveling her secrets through biomedical research is a difficult task, and its support requires long-term investment. The enterprise cannot tolerate wide swings in funding, either increases or decreases, or the phenomenon of roller coaster funding.

PREPARED STATEMENT

While the system must provide stability, it must provide opportunity for growth. It must provide opportunity for young scientists at the thresholds of their careers and a climate in which talented youth are motivated to choose careers in basic biomedical research. None of this can happen in a decrepid, obsolescent infrastructure. We must chart a path of stable, sustainable growth. For a Nation

of America's wealth, talent, and ambition, I believe that investment in the future should be unequivocal and nonnegotiable.

Thank you very much.

[The statement follows:]

STATEMENT OF DAVID KORN

Thank you for inviting me to share some thoughts with you this morning about the health of the biomedical research community, the adequacy of the NIH budget and the establishment of priorities for NIH spending.

The extraordinary success of the biomedical research enterprise in this country is the product of a unique relationship between our universities and the federal government that began more than four decades ago. The basis of the collaboration has been structured on the principle of investment, not of procurement, and the terms of the relationship have been straightforward: the government provides major financial support, particularly for basic research, while the universities produce knowledge and educate scientists in a conjoint process that is unique among the world's developed societies. The enterprise has grown and succeeded to a remarkable extent, and as one consequence, the principals have become exquisitely interdependent. Thus, the government relies heavily on academe to generate new knowledge and to produce future generations of basic and applied scientists who will maintain American pre-eminence in science and technology. On the other hand, a stable Federal funding policy has become crucial to the financial integrity of America's great research universities and critical to the strength of academic science.

The Congress has consistently accorded this collaborative effort a high priority, reflected even in the past difficult decade in the substantial growth of the NIH budget to $7.6 billion in fiscal year 1990 from $3.6 billion in fiscal year 1981. Despite this apparently robust growth of total NIH funding, NIH in the past few years has been cutting its support of investigators drastically, and cries of alarm resound throughout our research community. In the present fiscal year, the budgets of existing research projects will be cut about 12% from the levels previously approved after rigorous scientific and budgetary review; the budgets of new and competing research awards will be cut by 13%, on average. Cuts of this magnitude and extent, euphemistically dubbed "downward negotiations", have never previously been implemented; and, for all of that, NIH will be able to support only about 24% of the new and competing research projects approved

by hard-nosed scientific review panels. Thus, in this respect, too, fiscal year 1990 promises to be a record bad year.

These stark facts lead me to the conclusion that NIH spending, although substantial, is not at a level required for adequate support of this nation's biomedical research effort. The fiscal inadequacy results in part from a remarkable growth in the sophistication of the knowledge base and in the complexity of the technology, thus making the research effort far more resource intensive; ~~and,~~ in part, from a deliberate decision to extend the average duration of awards. Thus, commitments to existing projects in any budget year consume a larger share of the total available funds. These factors have contributed to what has been perceived as a "roller-coaster profile" of research support. Beyond these unpredictable fluctuations in year-to-year award rates, the chronic inadequacy of support for research training is a matter that should be of high national concern. In this year's appropriation, the Congress has prudently signaled its awareness of this problem by reversing the long stagnation of research training funding, which had been fixed at about 11,000 trainees a year throughout the past decade. Of similar concern is our neglect of the research infrastructure, particularly, the absence of Federal investment in research laboratories and complex equipment. In the present fiscal year, the Congress has appropriated $15 million for construction grants to be awarded competitively, primarily for animal breeding facilities. This is a commendable gesture, but one that is utterly inadequate to meet the accumulated needs. I strongly recommend that funding for research facilities be authorized and implemented under a generic NIH authority.

I urge that the Congress seek to achieve stable, reliable long-term growth of the NIH budget, recognizing the real costs of biomedical research, the importance of providing for continuing replenishment of the ranks of scientists and the need for safe, well-equipped laboratories and state-of-the-art technologies. I would like to examine these points further.

Sustainable Growth is Critical to Research

It may be useful to consider why the NIH budget is inadequate; I believe such an analysis offers two key lessons for research policy: first, we must recognize that biomedical research is expensive, and second, we must plan for sustainable growth in the NIH budget and for the expenditure of appropriated funds in a way that preserves NIH's flexibility.

Today's biomedical research projects differ vastly from those conducted as recently as a decade ago. Rapid advances in techniques and knowledge have led to greater specialization of research, to increasingly sensitive and costly research equipment, and to changes in the "fundamental sociology" of the research laboratory -- that is, to replacement of the small team of one or a few research technicians of limited scope by larger numbers of graduate students and postdoctoral fellows, who bring a remarkable expansion of "intellectual horsepower", diversity and creativity to any given research program. Accordingly, research projects tend to be larger and costlier. In addition, prices of the goods and services used in biomedical research have risen more rapidly than the general rate of inflation; the housing and care of animals ha added substantially to the costs of research that require the use of experimental animals; and, more broadly, generic environmental concerns have woven a web of regulatory complexity that has significantly increased the costs of the research enterprise, both in the direct and the indirect components.

In addition to the fact that projects have become more resource-intensive, the duration of grant awards has also increased. Such novel funding mechanisms as the OIG, the MERIT, and the JAVITS awards, all desirable innovations, have been greatly welcomed for the stability of support they offer to established investigators with outstanding track-records of accomplishment. This extension of terms of awards significantly reduces the costly administrative burdens that result from the flood of paperwork required by excessively frequent recompetitions that are otherwise required to permit even the most well-established and successful of our investigators to maintain their research programs. There is no question that the introduction of stability into the system

enhances the return on the research investment by reducing the costly efforts that are otherwise required to sustain specific investigative programs. However, these extended grant commitments inevitably increase NIH's out-year obligations, thereby reducing the proportion of funds available for new and competing grant awards in any given fiscal year.

The surge in the number of new and competing research awards to more than 6,000 per year during fiscal years 1985-1988 has significantly expanded the commitment base. The policy of establishing grant numbers in statute, also championed broadly by the community of research scientists, generated a bolus of continuing projects which must be funded, and it fostered the dangerous impression that the number of awards was the primary target that had to be reached without regard to consideration of the integrity of financial support for the individual projects. This excessive focus on grant number, in absence of consideration of fiscal consequences, creates an extraordinarily dangerous delusion regarding our national commitment to research support and has fueled the current rampant practice of "downward negotiations."

This pernicious practice deserves further comment. It is all too tempting to conclude that NIH's resource dilemma can be solved by a reallocation of existing funds or by establishing arbitrary caps on categories of costs. The costs of equipment, supplies, research staff and support personnel are market driven and generally lie beyond the control of individual investigators. Imposed cost-sharing ultimately forces investigators to cut back on the scope of their research programs, as they lay-off staff, reduce their use of supplies, cancel equipment purchases -- that is, as they are forced to engage in a series of defensive research strategies imposed by considerations totally foreign to the inherent logic of the research program itself. Let us be clear about one fact: in neither our research-intensive private nor public universities are there pools of dormant institutional funds standing by to absorb the cuts in Federal support; indeed, whether the alternative funding streams are student tuition, endowment earnings or ongoing philanthropy, such imposed cost sharing results in a

diversion of funds from other activities that contribute equally crucially to the support of a university's academic mission. To impair student support services, to divert funds from programs of undergraduate education, to starve our libraries or diminish programs of research and teaching in disciplines other than the natural sciences -- these are not acceptable strategies for responding to a conscious underfunding of our nation's basic science research effort.

I conclude, as I believe we must, that biomedical research is indeed an expensive investment, but one that has already yielded rich dividends and which promises to yield even richer ones in future years. When financial constraints lead to arbitrary cuts in previously approved research budgets and to award rates between 20 and 25% of approved grants, outstanding programs of research are aborted, and the Nation is the loser. For example, in the most recent funding round, the Cancer Institute was unable to fund a project aimed at studying the development of host resistance that leads to organ graft rejection. Among its potential outcomes, this project offered promising strategies for improving allogeneic bone marrow transplantation, a powerful new modality in cancer therapy. Another unfunded project would have used a powerful new DNA "footprinting" technique to visualize the binding of an important regulatory protein to genes in living cells; that research promised to provide valuable information not only about genetic regulation in general, but about the control of the human immune response to cancer, in particular. Such examples are legion within the portfolio of highly meritorious research grant applications, accorded high marks by rigorous merit evaluation, that miss the present-day paylines.

Instability in NIH support also sends a chilling message to investigators and students who might be considering careers in biomedical research. If we hope to maintain our national pre-eminence in science and technology, we must offer prospect of a reasonably secure career to our most talented students, who can evaluate a scientific career against other attractive options in law, business, computer science, etc. In the present research climate, make no

mistake about it, we are discouraging, not encouraging, talented youth who would be our leading scientific investigators and academic physicians in future years.

The appropriate course is to keep the NIH budget on a sustainable growth path that takes full advantage of the remarkable research prospects that have been enabled by prior Federal investments and now abound within the research community.

Make Training A Priority

Congress was wise to recognize the need for research training when it provided a 12% funding increase over fiscal year 1989. Clearly, the vigor of America's science enterprise depends crucially on the inflow in future years of well-trained investigators. Yet support for science education and training has stagnated at all levels of education, from the undergraduate through the postgraduate. The National Science Foundation has estimated that between now and the year 2000 we shall turn out 450,000 too few bachelors of science and 100,000 too few Ph.D.s in the natural sciences. At the same time, several studies have pointed out that the aging of the cohorts of faculty members who were recruited in the 1950s and 1960s will require replacement by new faculty hires if the research and training enterprise is not to falter. Yet, NIH spending on research training has been chronically underfunded in the past decade, with the number of trainees fixed at about 11,000 each year. Congress should continue to assign a higher priority to research training in fiscal year 1991 and later years; however, that priority can again not be managed simply by engaging in "numbers games." The development of a sustainable program of research investment must be put in place if bright young people with diverse career options are to be led to the choice of an arduous and demanding research career.

Construction Costs Are Prohibitive for Research Universities

The absence of direct Federal construction grants seriously confounds the capacity of universities to plan for their own participation in maintaining the

vitality of biomedical research. It is disappointing and frustrating, but nonetheless true, that research laboratories built in the 1950s and 1960s are, less than 30 years later, poorly configured and inadequately capacitated to support contemporary biomedical research in conformity with federal, state and local environmental standards. Surveys conducted by the National Science Foundation, the NIH and others have repeatedly documented the problems with our existing stock of research buildings. At medical schools, for example, almost half of the existing research space was judged to be inadequate; similar inadequacies were recorded at independent research organizations, colleges and universities. Changes in the knowledge base, the technologies, in animal care, in building codes and in environmental regulations -- all have contributed to this phenomenon of rapid obsolescence.

Research universities have attempted to address their facilities needs, but without direct federal assistance, the costs become prohibitive. NIH, in its 1988 report, "The Status of Biomedical Research Facilities," stated that research universities, including medical schools, expected to add 12 million net square feet of incremental research space during 1986-89. Among medical schools, private funds, debt and internal school funds were expected to provide 85% of the financial needs, with federal sources contributing only 5%. Medical schools thus expected to incur almost $600 million in debt, yet those projects represented only 40% of the recognized need for new research space! In the absence of an NIH construction program, universities must seek to recover facilities expenses through indirect costs, but given the difference in cost of money alone, it is clear that the indirect recovery mechanism is more costly with respect to its call on federal funds than would be a program of up-front federal funding. Finally, with regard to the indirect costs of research, it has been shown clearly that the largest and most rapidly increasing component of those costs is related to facilities, and it is the facilities component that largely explains the difference in average indirect cost rates between our private and public institutions.

Direct federal support is urgently needed to supplement institutional, private and state funds.

Conclusion

The long record of federal investment in biomedical science has made possible a remarkable transformation in the knowledge base and the sophistication of research. That transformation entails a marked change in the resource intensity and cost of biomedical research, which exceeds the rate of general inflation in the economy. Specific policies adopted in recent years have limited the amount of funds available for competing grant awards. I believe the NIH budget should reflect the changing resource intensity of research, enabling NIH to eliminate the "roller coaster" effect in the future. In trying to assess the "correct amount" for the NIH budget, we should approach the problem as one involving an investment decision in the nation's future. We should select a rate of growth that will meet the long-term requirements of America's research enterprise, including the need for training and for assistance in maintaining a state-of-the-art research infrastructure, and will maintain America's position of international leadership in science and scientific education.

FEWER RESEARCHERS ENTERING FIELD

Senator HOLLINGS. Man, that is wonderful, unequivocal, nonnegotiable. This is a good hearing, isn't it? [Laughter.]

We usually hear a diversity of opinions on these panels. You folks sound like the Andrew Sisters. [Laughter.]

I am hearing one tune throughout, specifically, the attraction of the young minds into research. Each of you have emphasized that it is just not working at all and we are losing ground. Dr. Busch, you were pointing it out originally. Can you elaborate on that and give us some statistics on how many students are coming in and what has caused the dropoff?

Dr. BUSCH. First of all, I would like to harken back to President Coolidge, who pointed out that the business of America is business, and in the product development field, we have been woefully short.

I bought this watch in Japan. You can't buy one like this in the United States. There are a lot of things that you can't buy that are made in America. One of the things that we want to do, buy more research that will be an investment, and I would like to make a couple of points or comments on that.

Second, my dad taught me that you get what you pay for. Ultimately, if you hire a $17,000 a year doctor, you have got a $17,000 a year doctor. If you hire a $150,000 a year doctor, you have got a different kind of doctor.

Senator BUMPERS. Maybe a $50,000 a year doctor.

Dr. BUSCH. You won't find many of those in Texas.

Senator HOLLINGS. Arkansas. [Laughter.]

Dr. BUSCH. Yes, sir; I apologize. I think if we are going to attract young physicians and physician scientists, M.D.-Ph.D.'s into this complex area and the insecurity that Dr. Korn has pointed out, and I am an M.D.-Ph.D. of many years' duration, we are going to have to make a fiscal statement to them.

They are not going to come for $17,000 or $11,000 a year. I think that what Dr. Hseuh has said so articulately about the vast reduction in medical physicians-scientists is something that is absolutely crucial. I am a Ph.D., and I earned my Ph.D. the hard way, at the University of Wisconsin under very strict leadership, I must say.

I have great respect for all the Ph.D.'s, but they don't understand the medical problems. It is these fellows who have the training, the residency, the internal medicine, the surgeons, the eye people, all the hard-working gentlemen who serve our public so well, they understand the problems, and they are in the position to make patient to patient evaluation, but that population is dropping from 5 percent to 2 percent to one-half of 1 percent. We can have this vast body of knowledge; it just won't impact on our patient population.

So Senator, I can't give you numbers, and I don't even know that the numbers are so relevant. We are losing the enthusiasm, and we are losing that quality of person that we have to have.

DRUG DEVELOPMENT

Senator HOLLINGS. You tell us molecular biology is so developed now that there are gaps in the pharmaceutical industry that they don't know how to contend with. Elaborate on that, for us, because what we have are dramatic developments in basic science and the research endeavor, yet the drug industry doesn't even know how to approach the subject.

Heaven knows, we ought to know more about it.

Dr. BUSCH. Yes, sir; and let me say that you can't pick up a journal, either in the medical specialties or the biochemical specialties or the journal Nature or any other major journal and not be confronted with the vast evolution of our understanding of all these little nucleic acids and how they impact on us human beings.

You gentlemen have supported the genome project, which some day will tell us all the genes we all have and how we all fit together. But I am concerned about quite another aspect, and that is, to take that information base and put that into drug development.

Industry lacks the resources. You may appreciate that if you take the combined resources of American pharmaceutical industry, they are far smaller than the resources of the NIH for basic drug development. Merck & Co., Lilly & Co., all the great companies of this country do not have, combined, the dollar input into research that our Government puts into the National Institutes of Health.

They have to put their money where the best bed is for the quickest product, but we as a nation are competing with people looking down the road 25 and 50 years from now. Dr. DeBakey came to visit the other day. We chatted on Saturday morning about the Japanese groups who came to visit with him. They said:

> Fellows, we are doing development on the heart that is going to take 25 to 50 years to make money.

And they said:

> Fine. We are glad to put money into this. We have got to look for 25 and 50 years. We have plenty of products now. We are looking for these 25 and 50 years from now.

So this translation of this vast body of information that has accumulated into drug development, I think, has to be a public function. When we get on the right track, we can let industry come in, make the profits, pay the taxes, benefit the public, but there is a void, and the void has to be filled by us, or somebody else is going to fill it for us.

I am deeply concerned about that.

Senator HOLLINGS. I am going to yield to my colleagues, because we have got a wonderful interest here this morning, and they have more important questions, but how do we avoid this charge? This Government here, and particularly this administration over the past 9 years—including President Bush, says, "Let's get rid of the Government. Let's get the Government out of industry and let the industry do it."

You can see that question in Senator Stevens' mind about private research. How do I get in and compete with Eli Lilly or whoever it is? I mean at the Federal level now.

Dr. BUSCH. We don't want to compete with private industry, sir. I am 100 percent in favor of private industry. What I want us to do is to translate the information up to the point that product development is meaningful and then turn that to industry. Let them take advantage of the patents and the developments and produce the drugs on a national scale and sell them and give the proper revenues to our country, and hopefully, we can have drugs that sell $1 billion a year, like many do, and offer revenue to our country and pay off some of this hideous debt that I am very concerned about for my eight grandchildren. Who is going to pay that $3 trillion?

Hopefully, our scientific developments will give us the entree into markets that will be worldside markets and put us ahead of other people.

Senator HOLLINGS. Let me yield to our chairman. I should have originally. I am sorry.

NIH APPROVAL OF APPLICATIONS

Senator HARKIN. I am sorry. I should have left. I just have one question, one that is plaguing me. I want you and other panelists who are going to come up to think about this.

NIH approves over 95 percent of the grant applications that are submitted to it each year. Every year since 1972, with only two minor exceptions, NIH has approved an ever higher percentage of grant applications. Get this, Senator Hollings.

In 1972, the approval rate was 69.9 percent; in 1982, was 84.7 percent; the rate for 1990 is expected to be 95.3 percent.

It almost seems that what is happening is all these things are coming through NIH; they rubberstamp it and then they dump it in our laps, and we are supposed to make some decisions on these things. When everything that comes through is approved, what are we to expect?

Senator HOLLINGS. I am getting a different story, that there is a declining rate of approval.

Senator BUMPERS. Are you talking about approval of applicants?

Dr. HSUEH. There is two issues: One is approval and two is funding. Approval means, yes; this is worthy of being funded, but what is actually funded is the numbers on the front of this chart.

Senator HARKIN. What I am saying is that NIH is saying that this is a greater percentage.

Senator STEVENS. That is relative to the amount of money that is sought, don't forget. I want to get into this, too.

Senator BUMPERS. We are like ships passing in the night here. Let's be sure we are all talking about the same thing. My information is that this year, NIH will only fund about 24 percent of the approved grants that they would like to fund.

Senator HARKIN. Of the approved.

Senator HOLLINGS. What about it, Dr. Korn?

Senator BUMPERS. You are saying that they approve 90 to 95 percent, but they only fund 24 percent; is that it?

Senator HARKIN. There you go; yes; that it is.

Dr. HSUEH. That is exactly it.

Senator HARKIN. But I am saying that in the past, NIH didn't approve that high of a rate. It used to approve somewhere in the 60-percent range, 60- to 70-percent range, so that our funding level was higher. Now they approve everything that comes through and it is down to 20 percent funded.

Dr. KORN. Senator, could I try that one? I think what you are looking at has to be looked at as though you were, let's say, a professor teaching a course and you have a population of students that are being evaluated.

There are a lot of different ways you can hand out your grades. You can grade on a strict curve or you can decide that, as my son tells me, that 15 percent of the kids in the class are going to be bounced out as a matter of policy, this, that and the other thing. Over the years, and I have been on NIH study sections since about 1972 or 1973, there has been a change in the philosophy of what is the requirement for disapproving a grant?

In other words, there has been a time in the seventies when, if something weren't considered pretty good, it would get a disapproval; in other words, a lot of F's, failures. More recently, starting in the late seventies, the idea was put forth and established that if you are going to fail something, to hear that your proposal has failed is really pretty insulting and devastating, even to a duncy proposal.

So you don't use that mark unless it really is, like poronography, without any redeeming merit whatever, OK? So you use E or E minus or D's, C's, B's and A's to get a spectrum of merit out of a

pool of competing proposals, just like grading exam papers or something.

You can decide you are only going to flunk things that are really terrible or you are going to flunk things that I might call a D plus; you call it an F, and that is what the debate is about with approvals and disapprovals, you see.

Senator HARKIN. Except there is a difference.

Senator BUMPERS. Tom, would you yield a second? Here is a chart here that everybody ought to have. This chart shows, this top figure here, of those that they reviewed, and that is about 19,000, almost 20,000 they reviewed last year, here is the ones that were eligible, about 17,700, and here is the ones they awarded.

Senator HARKIN. Funded.

Senator BUMPERS. That is the 24 percent.

Senator STEVENS. That funded.

Senator HOLLINGS. We funded. Yes.

Senator BUMPERS. We funded. You can see this chart across here, and you can see all these. The number of applicants has been going up; the number reviewed has been going up and the number of awards has.

Senator STEVENS. But that doesn't show who funded some of the rest of them. Some of the rest of them were funded with moneys contributed by nonprofit corporations. There is an indirect cost.

Senator BUMPERS. I didn't realize that.

Senator ADAMS. Mr. Chairman, I just want to mention, while I have both chairmen here, that over the past 2 days, I have listened to 55 different witnesses from opthalmology to diabetes and so on on the point of medical research, and one of the factors that they are stressing is that there is a window in time now, with molecular biology coming on line, and that a number of these grants that we are talking about, that they are now knocking out the younger people, the younger researchers from receiving their grants because the older ones have a track record and so on.

That is accounting for the fact that a lot of pressure is on younger people not to go into the field. That is part of what the group is saying. I heard it all the way from arthritis to diabetes, and I will say this: They have agreed upon a funding figure, an ad hoc group, all these people, and they were from every field, about what NIH should have in order to create the programs that you are talking about.

I just wanted to say that or I just wanted to echo what they were saying from listening to all these people over all these days and just to thank you for holding this hearing this morning, because it is a key factor. We don't have much time because this science change, this whole new way of looking at genetics and so on is for the young. It is in the digital fields as well as in the medical fields, and they need to have some of the younger people funded, too.

So I hope that this will be developed. I am sorry. I have to go to another appropriations meeting because I took the time from that to do this the last 2 days. Tom, your witnesses were wonderful.

Senator HARKIN. Thank you.

Dr. BUSCH. Senator, could I just make one comment? In part, it is a tribute to the wisdom of our government for training so many excellent young people that the proposals that they are writing are

outstanding proposals compared to what I saw when I started in science back in the late forties. These young people are proposing superb approaches to scientific problems, and we can't fund them because the money isn't there. The 95 percent reflects the excellence of your endeavors.

Senator HARKIN. A lot much better than it was 15 years ago.

Dr. BUSCH. Much better than it was ever before.

Dr. HSUEH. I would just like to point out that over the last several years we have tried to maintain the total number of grants stable at around 28,500. That is RO1's.

The problem is that a few years ago, we attempted to improve the situation by funding 6,500 new and competing. Well, now, several years later, we are only funding 4,500 new and competing, so despite the marked increase in knowledge and technology, we are funding 2,000 less grants this year than we were several years ago.

The question is, how to get some stability so that people like us know what to expect. How can we maintain some level of consistent funding?

GROWTH IN GRANT AWARDS

Senator HARKIN. Let me throw some other figures in there. Average length of grant awards has grown steadily for the last 15 years. It was at 3.2 percent in 1972. It is now up to 4.3 years in average length. So we have kept those up.

Also, the average size of grant applications grew from $206,000 to $232,700, a 13-percent increase just in 1 year, just in 1 year. So these grants that are being awarded are costing more money; they are taking longer time; they are going higher than the rate of inflation and you wonder why we can't get new grants for new and competing proposals.

I am saying a lot of things are happening out there that I don't know if I understand.

Dr. RYAN. If I could respond maybe to the length of the grant issue, because again, having had the privilege to be on the advisory committee to Director of the NIH when that was debated at that advisory council, it basically came down to, when a grant goes for 3.2 years, Senator, the situation is, particularly for the first time in, for a grantee, one of these new scientists, if they are fortunate to get it the first time around, the reality is, before they finish the first year, they have to be writing a grant to be renewed. That is truly not an exaggeration, because it takes one year in the review cycle which you are dealing with out at that particular end, and it takes you that time to start up your laboratory.

So it was felt that both because of scientists not being able to be doing research because they really were doing grantsmanship and preparing grants, as well as the impact on study sections, it was felt that 3 years really wasn't an adequate time. That was a significant part of the rationale and the NIH at the highest levels, I think, made a wise decision with that in mind.

To come back to the issue of molecular biology, in my opinion, it really is the most profound impact in biology. It is more profound than what computers have done to engineering, mathematics and

physics in terms of the impact and the tremendous opportunity there is for us today.

Again, not to speak for chauvinistic reasons about opthalmology but because it is something I know, what people have been able to do is to define the gene for retinoblastoma, to be able to actually see how this gene works and how you can change the cells back to normal in tissue culture, to show the gene where retinitis pigmentosa, the leading inherited cause of blindness, is located, and again, to show now in laboratory animals, in rodents, that they are able to actually transplant these RPE cells, retinal pigment epidelial cells, tremendous opportunities are there waiting for us.

Again, it just would be such a tragedy if we missed the opportunity, and it is on these young scientists, and I can tell you again, just to echo the comments we have heard, I was so fortunate to get in when I did, some 20 years ago. I couldn't get in today. You have got people out at our department now with M.D.'s, Ph.D.'s, from Harvard and Hopkins, the best students, the top students in their class, literally who are in their third grant revision going around.

That is 1½ years of writing grants, and that is not atypical.

Senator HARKIN. Thank you, Mr. Chairman.

Senator HOLLINGS. Good. Thank you. Senator Stevens was waiting.

PRIVATE SECTOR COMPETITION

Senator STEVENS. I have got to get back. I am supposed to be at another subcommittee myself. What do you pay these young scientists you are talking about? In their grant is their own pay, right?

Dr. RYAN. That is correct.

Senator STEVENS. What is the level of pay?

Dr. RYAN. I will give you ranges, if I could, Senator, in that regard.

Senator STEVENS. I am interested in specifics.

Dr. RYAN. I will be very specific. If we have an assistant professor in our department who is a basic scientist with a Ph.D., that individual salary will range from $35,000 to $45,000 and will be covered in significant part on a grant.

If you are talking about the postdoctoral trainees that we have for $17,000 or sometimes less than that, and I can tell you very honestly that from my own research funded with RO1 grants, a very good strategy for me has been to take students from Germany or Japan, funded by their countries, to come and do that research just because of the impact that it has on the individual grant.

So those are what I would be doing, talking very specifically to you salarywise. A dean would have a better perspective, perhaps.

Senator STEVENS. I can't really stay. We went into this in Governmental Affairs, as I told you. We found that at NIH, more than one-third of the desks at NIH were vacant. You talk about how they are not really reviewing grants the way they used to in NIH; they don't have the manpower. They are not keeping people. The people are moving out and going in to the nonprofit corporations that are associated—and most of you running nonprofit corporations are associated with the universities. At least that is what we found, is that most do.

The salary level is much higher in those nonprofit corporations than they are at NIH. Do you think there is a role for us to finance in-house research at NIH?

Dr. RYAN. Yes; I do, Senator. I would just say that——

Senator STEVENS. How do we do it if we can't match the salaries you are paying?

Dr. RYAN. If I could say two things: One, in vision research again, only because I know it well, there is an extremely cooperative complementary, with an E, relationship between the intramural program at the National Eye Institute and what goes on in our extramural community of universities.

Specifically, the NEI is focused on epidemiology; it is focused on immunology and has brought together expertise in large groups.

Senator STEVENS. I understand this, and I have come through it. What do you do about the money? You are not looking at money. My father was blind. If I could give you the whole Federal budget, I would give it to you. It is not a question of our support; it is a question of how we do it with the mechanisms we have now.

You are paying much more out there in these nonprofit corporations than we can pay in government. Don't shake your head, Doctor, because it is true. It is the same thing in the law firms. If you want to go to New York and be a first-year person in the law firm you get $80,000. If you want to come down and work at the Department of Justice, you get $29,000.

That is the competitive range we have in your institutions, too. I can't understand how your profession looks at the breakthrough of where should people go when they are highly talented and how we get them there. We had Norton Simon and a few others, Dr. Hammer. We have had specific support from specific individuals to continue research in NIH.

You want more of government money to continue research in your organization, but you have some nonprofit support out there, too. It is not reported in your chart.

I close by saying, and I would be glad to have you print it. That has nothing to do with dollars. That is the number of applications that have been funded and the number of the applications that have been approved has gone up geometrically, so that the number that we are actually funding comes down, although the amount of money continues to go up.

This is not in relation to how much money we put in research as far as Federal money. My problem is: How can we continue to keep an in-house research at NIH and fund your research at universities if both of us have to compete with the private sector research funding level in terms of salary levels?

That is what it is. If your profession really wanted to see this thing work, in my opinion, and I am being critical of medical professionalists, you would find some way to get us competent people in NIH to fill those desks, because that is one of the problems. We keep moving people through.

Warren Magnuson used to say that the busiest person in NIH is the sign painter; he is changing the names on the doors. They are going through too fast. They are not getting the kind of residents that they used to have in NIH. As a consequence, every application

comes through as approved, and as a consequence, we are funding fewer applications.

I think that is part of your profession's problem, not just ours. We are politicians, but you people have to find some way to get competent people into the areas where they are reviewing these and also get us some understanding of how to keep the salary level that the taxpayers can afford in the research area. If you take the same person that is getting $60,000 in NIH and turn them into an employee for a nonprofit institution and double his salary, do you know what happens? More people want to leave NIH.

It is not just getting more research done; you get less. Somehow or other, we have to stop this cycle, and I don't know how to do it, but I think your profession has as much responsibility to it. You are bringing it to us; I am giving it back to you. I really think you have the responsibility to see to it that we find an answer to: How can we attract these young people into your profession with some Federal money and some nonprofit, nontaxable money and some private support, which I am glad to hear you say you support, Doctor.

But it is not as easy as just asking for more Federal money. We have given you increasingly more Federal money every year, increasingly more every year. But it is doing less; it is accomplishing less because we are having this tremendous acceleration in the cost of research in terms of manpower. That ain't my problem; that is yours as much as it is ours.

Senator HOLLINGS. Dr. Korn?

Dr. KORN. Senator, there are just so many issues that are all involved in the point you are making. I think, first of all, that NIH salaries do not have to be competitive at the point of parity with outside NIH salaries. They have to be somewhat realistic in terms of their relationship, as any other salaries do in a free market or a free-labor-market economy. We don't have forced labor in this country. People will go, but there are other advantages to working in a place like NIH.

People who wish that environment, a full-time dedication to science with almost no other distractions in their day-to-day and week will to week activities, I don't think they are demanding parity with the world outside, but some reasonable relationship, and I think the problem is worse at the more senior levels and not at the junior intake levels.

I do not believe there has been a problem bringing young people into NIH. I think the problem is that when they succeed and do well, they get a lot of attractive offers from the competition, and they may choose to take them as their families grow and so on and so forth.

Senator STEVENS. I agree. You are right.

Dr. KORN. I don't think that is a big problem. I think there has to be some relief on the upper levels of medical scientists' salaries in the NIH, and how you all choose to do that, I don't know, but I don't think it is a mega problem. I think it is a very attackable problem.

The other point I wanted to make is that you, several times, made the comment that you believe that the biotech industry or private industry is doing basically the same work that is being

done in universities and NIH, and I don't think that is true, with all respect.

I believe that the point of an industry is to develop a particular portion of knowledge or materials that can turn into some kind of marketable product. They are not into basic science. There is a time perspective in basic science by its very definition that private industry has a real hard problem in this country coming to grips with, and it is one of the reasons why we have lost our competitive advantages in so many of our industries, because it is short-term, bottom line orientation.

That is exactly the opposite of what basic research is about. Basic research is long-term orientation. When I started out, Senator, the hot areas that I worked on were in the field of genetics and little tiny viruses that infect bacteria; not animals, not people, bacteria. We were interested in how bacteria exchanged genetic information; How do they mate? And we were interested in funny chromosomes and bacteria that became interesting because they carried antibiotic resistance.

Those very obscure kinds of research that no industry in the world would have touched are the basis for the whole recombinant DNA technology that we benefited from, those very obscure dust bin kinds of problems, industry wasn't going to support. Industry didn't care how two ecoli mate. They really didn't care about whether or not bacteria had a bunch of funny little circular DNA molecules that they could pass around almost epidemically. Nobody was interested in that stuff.

That is the basis of retro viruses; it is the basis of cell transformation; it is the whole basis of the biotech industry. That is where public investment is needed.

Senator STEVENS. I said that I think you do have competitiveness, though, in terms of personnel, and we have a trend from—and I don't care if it is your industry or all of them—from Government to a private research base to a public-supported, private-entity-supported kind of continuation of that. We see, or I, at least, see a movement of people through those sectors.

The problem about maintaining the first ought to be our primary problem as members of the Government of maintaining NIH. I find it is not possible to give NIH the support it wants because the competitive factor is, in fact, that nonprofit corporate research sector, which you are all part of, and the increase in terms of compensation that you are paying. We can't keep people there anymore, as a consequence, we are, in fact, getting less in-house research done unless your profession believes we shouldn't have a special interest in in-house research as we used to have. I don't know.

But it is still not possible. I don't think we can, under the current structures of government, pay them what they can earn in the nonprofit sector, not in the private sector, but the nonprofit.

Dr. HSUEH. I agree with Dr. Korn that it is not necessarily so much parity in salary, but it is the little things that count. It used to be easier for them to get equipment, to get supplies, to pursue a new idea and they didn't really have to——

Senator HARKIN. You are right. The questions I asked earlier you gave good answers to in terms of the grants that students are brighter; the learning curve is much higher; the kind of investiga-

tions they are going into do take longer because there is more intricate than they used to be.

The other thing is that in terms of getting the equipment and the kind of support these people need, sometimes they are into it and it takes them 2 years down the road before they get it——

Senator STEVENS. I agree with that.

Senator HARKIN [continuing]. Before they get the equipment. I heard an ad on the radio this morning for McDonnell-Douglas. There have this series of ads running on the radio, and it is about how they have this teamwork and if they had a problem with a missile how the fin would work, and they got together and they figured it all out and they got it to work, right? I bet you that he didn't have to wait 2 years to get the kind of support and materials that he needed to figure out how to put that fin on that.

Senator STEVENS. That is right, but that is still NIH budgeting.

Senator HOLLINGS. We have waited 2 years for Senator Bumpers to ask his question. [Laughter.]

I appreciate it. The Chairman is going to yield to Senator Bumpers. We have two other important panels here.

Senator BUMPERS. I never went to the Armed Services Committee, because I never got to ask a question. There were so many in front of me. [Laughter.]

INVESTMENT IN R&D

Ted, before you go, I want you to listen to this. It will take about 15 seconds. This is from the New York Times a couple of weeks ago.

> For the first time in 14 years, spending on corporate research and development in the United States hasn't even kept pace with inflation, raising concerns that the Nation is lagging in its efforts to hold a competitive edge in high technology. Many corporate research executives say the decline is particularly troublesome because at the same time research money is increasingly being shifted from basic research to development of specific products, reducing chances of fundamental break-throughs. What's more, they say, a smaller portion of research is being done in large laboratories where resources can be pooled, limiting the opportunity for significant advances.

It also says:

> Experts say Japanese companies, flush with cash, keep increasing research spending at a brisk rate. As of 1987, the most recent year in which comparative figures are available, the growth of research and development spending among Japanese companies was more than three times that for the United States companies statistics from the "Organization of Economic Community Development" show.

Now you can leave. [Laughter.]

Senator STEVENS. The trouble is, if you ask questions around here, you are automatically deemed an opponent. You have to understand the analysis of where we are. Incidentally, the Japanese just lost 28 percent of their equity value in the last 6 weeks. I don't think they will be spending like that in the next 10 years.

Dr. BUSCH. Yes; they will, Senator.

COMPARABLE SALARIES

Senator BUMPERS. Ted, there is one other point I want to make. You kept talking about NIH, and I think this panel will agree that the most basic of basic research is done at NIH. You talk about:

How are we going to compete? They have not recruited a senior scientist at NIH in 3 years because of salary and other concerns.

Senator STEVENS. That is what I was asking.

Senator BUMPERS. Of course you are not going to compete with the private sector as long as you do that.

Senator HOLLINGS. Forty years ago? Dr. Busch, you were talking about 40 years ago. Was there parity in the early fifties, let's say, 30, 40 years ago between the private salary and the NIH salary?

Dr. BUSCH. Forty years ago, sir, salaries at the NIH were so good and the opportunities were so great, you couldn't keep people out of there with a baseball bat, and I tried, very hard to go to the NIH from the University of Wisconsin. I had to settle for Yale University instead, which wasn't anywhere near as good at that time.

I think what has happened is we were the New York Yankees back in the forties. Where are the New York Yankees now. They are not in first place. Oakland is in first place; Japan is in first place.

Senator HOLLINGS. Is that in the bush league? [Laughter.]

Excuse me, Senator Bumpers.

Senator BUMPERS. Mr. Chairman, I know all the answers to all my questions, so there is really not much point in asking them. [Laughter.]

YOUNG RESEARCHERS

But I do want to ask this question: Are our best students going into biomedical research?

Dr. BUSCH. They are going into law, and they are going into business, and the salaries in law, which were alluded to earlier, and I have one of my family in law in New York City who is getting $160,000 a year, and she is 35 years old.

I know people who are getting equivalent incomes in business administration, in the market and others things. Why should anybody go and take a job for $35,000 a year with an M.D. and a Ph.D. with all this harassment by these committees in cutting your budget and then cutting your award and applying every 3 to 4 years with the jeopardy of whether you are going to grow or you are not going to grow and not take a job that is going to be lucrative?

I think you are going to get what you are going to pay for.

Senator BUMPERS. My question is: Are all the brightest medical students, for example, going into research?

Dr. BUSCH. They are not.

Senator BUMPERS. They are not?

Dr. HSUEH. It is increasingly harder to fill our fellowship slots and research positions, and this has raised the issue, at least within internal medical circles, continually.

Senator BUMPERS. Dr. Korn, did you want to comment on that?

Dr. KORN. Sir, I think that the problem is really not so much the income salaries. I think it is the perception of instability. You don't make your career in a crap shoot with a 20-percent chance you are going to win, and if you don't, you are out of a job. That is really where the problem is.

Senator BUMPERS. How would you explain this?

NIH tells me that despite their inability to attract senior scientists at that salary level, they have been able to fill their positions with junior scientists who come in there at very low salaries and work their way up to senior scientist. Whether the quality is as good or not, I don't know, but they say that they have not really suffered all that much for senior scientists because they have been able to attract young scientists who work their way up to senior scientist.

Dr. KORN. I don't think it is that big of a problem, as I was trying to discuss with Senator Stevens. I think there is a problem with the upper echelon of established investigators at NIH and that a relatively, by your standards, modest adjustment in the funding, we probably could solve that problem in terms of providing a reasonable opportunity of income.

I don't think it is a problem at the lowest levels, and I think that some turnover of personnel is healthy for organizations, besides.

I think that to the extent that NIH provides a corps of superbly trained, bright, creative investigators who go out and populate our institutions and help turn on other young people is a good thing; it is an advertisement. I wouldn't want them all to stay in NIH until they died. I think that would be terrible.

Senator BUMPERS. So you think the turnover is appropriate.

Dr. KORN. To a point, yes, sir.

DOWNWARD NEGOTIATIONS

Senator BUMPERS. Let me ask one other question. Dr. Hsueh, let me ask you. This negotiating downward of the grants, is it better to fund more programs by negotiating downward, or should we fund fewer fully?

Dr. HSUEH. You are asking a person who just got a 13-percent cut and now expects a 25-percent cut, and I am trying to decide, well, what science do I cut out? What experiments will I not be able to achieve?

I think that is a very difficult question to tackle. I feel that we have to maintain some number of grants that are fully funded.

INTERNATIONAL COOPERATION

Senator BUMPERS. Is there room for some international cooperation? For example, if we were to set up some sort of international biomedical research system with Germany, Japan, and the more developed nations, instead of each one of us repeating the same research, is there room for international biomedical research through cooperative ventures and so on?

Dr. BUSCH. It goes on all the time.

Senator BUMPERS. Pardon?

Dr. BUSCH. The NIH, over many years, has supported and participated in research in many countries in Europe and Asia.

Senator BUMPERS. Are you telling me we fund grants?

Dr. BUSCH. Yes, sir; we have.

Senator BUMPERS. In those countries?

Dr. BUSCH. We fund grants; fund people; fund clinical research, many things.

Senator BUMPERS. Should we do more of it or not?

Dr. BUSCH. Not for my money. I want the money here in the United States. That is where it belongs.

Senator BUMPERS. I want the research done.

Dr. KORN. It is a different kind of environment. I bet most of us are inundated with applicants from foreign countries for young people with both Ph.D.'s and M.D.'s to come train with us. Our problem is making selections and turning them back.

There is no other country that provides a research training environment like an American research laboratory, Senator. It doesn't exist anywhere in the world. People come into our places, and they are blown away by the skepticism, the curiosity, the nondogmatism, the nonhierarchy, the no-hurt professor who tells everybody what they are going to do every day.

I have a colleague at the University of Tokyo you might know quite well, a very talented young man making major contributions to a field that I have been working in. A new chairman came into his department of biochemistry and told him he would no longer work on his life time work because the chair professor decided that the whole department was now going to do another kind of work.

It is a very chilling atmospheric for young people. That is why they want to come to us.

BASIC SCIENCE RESEARCH

Senator BUMPERS. Let me ask this panel this question. Here is a chart that shows, comparatively, the NIH research in dark; this small segment is other Federal. From here to here is industry; 45 percent of all health R&D is industry, and then here is other. There is some State investment in that, and I don't know what the other is.

You can see that industry is putting up 45 percent of all the research dollars and NIH is putting up 33 percent, 12 percent less. Isn't it the truth the private sector is more involved in applied research than they are in basic research? Isn't that the question?

Dr. KORN. That is exactly right.

Dr. HSUEH. Yes.

Dr. RYAN. Yes.

Senator BUMPERS. Industry is looking for something they can get on the market and make some money out of.

Dr. KORN. It is little r, big D.

Senator BUMPERS. You just took the words out of my mouth. But isn't it fair to say, then, that if the United States is going to keep anything like a lead, we have to invest in basic research? I have heard that the Japanese are overtaking us now; is that not true?

Dr. BUSCH. Yes; it is.

Senator BUMPERS. It is true?

Dr. KORN. Well, they are catching up, but I think we have the lead, I do.

Dr. HSUEH. We still have it.

Senator BUMPERS. Incidentally, with these research grants, when they have a breakthrough, is that all immediately available to the private sector?

Dr. BUSCH. Yes.

Senator BUMPERS. Do they get the benefit of our basic research.

Dr. RYAN. Yes; it is.

Senator BUMPERS. Free?

Dr. RYAN. Published free, and they encourage and would want things to be patented so that the industry can then take it through the FDA process. That another aspect to deal with is: How long does it take to bring a product to the patient?

I think the key, as you are saying and implying, Senator, is: How do we get the basic research as funded by the Government and through the NIH and extramural community and then through the applications or applied research in industry, and then to the public and the patient?

That is ultimately what we want, and how to keep that together, Senate Hollings, in your opening remarks you so appropriately made, look at what is going on across the Pacific. We can't afford to lose this industry; we just can't afford it nationally.

Senator BUMPERS. So the bottom line is that if we don't fund NIH, the basic research is not going to be done.

Dr. RYAN. And you are going to cut off the whole future.

Senator BUMPERS. Thank you, Mr. Chairman.

Senator HOLLINGS. Thank you all four. I could go on all day long.

Senator BUMPERS. I could, too. This is a very interesting hearing.

Senator HOLLINGS. This is very interesting, and we have got another important panel. We will keep the record open for further questions, if we can submit them in writing to you. Thank you each very, very much.

STATEMENT OF ROBERT DRESING, PRESIDENT AND CHIEF EXECUTIVE OFFICER, CYSTIC FIBROSIS FOUNDATION

Senator HOLLINGS. We have panel No. 2, Mr. Robert Dresing, the Cystic Fibrosis Foundation; Ms. Andrea DiLorenzo, National Coalition for Cancer Survivorship and Ms. Abbey Meyers, the National Organization for Rare Diseases.

We believe in ERA, and we will start with you, Mr. Dresing.

Mr. DRESING. Thank you very much, Senator. I appreciate very much the opportunity to be here today. Let me say at the beginning that having heard the testimony this morning that has been given that this is going to be a lot tougher job this morning than I thought it might be.

Senator HOLLINGS. Incidentally, your full statements will be included in the record. Please summarize. As our Chairman Harkin so aptly said, give us two or three things that we have got to know about and center our thoughts and wonderment on so that we can really approach what you are trying to get over to us.

Mr. DRESING. That is fine, because I want you to leave with one thought, and that is that biomedical research is not a priority in the country by any standard that you want to measure it by, it is not, and by any fact that justifies that it should be, I believe that it is.

I am going to give you some examples of why I think that it isn't. We are talking here this morning about an expenditure at NIH of $7 billion, and that is not a small piece of change, but when you look at what that $7 billion is providing and the opportunities that it has to give us a return on investment, it is a pitifully small, I believe, an obscene sum of dollars.

Some $7 billion begin to address the needs of this country from a biomedical research standpoint, and if you want to look at it not from the standpoint of what might it do for the quality of life of individuals of this country, which we are supposed to be charged with providing for, but let's look at it from an economic standpoint.

This country is on the verge of picking up a check for $700 billion to take care of the constituents. That is what it is going to be for the health care costs of this country this coming year, and yet the dollars that could be invested to stop the flow, to solve the problems, to give us the answers, is $7 billion.

Senator HOLLINGS. The health care costs in America——

Mr. DRESING. Is approaching $700 billion.

Senator HOLLINGS. I thought you were going to tell me what about the savings and loans. Thank you. [Laughter.]

That has gotten up to $360 billion. Go ahead.

Mr. DRESING. Isn't that amazing?

Senator HOLLINGS Isn't that amazing? That is a total waste.

Mr. DRESING. That is absolute total waste. If we are talking about just the efficiencies and what we can do with research dollars to stop this flow of costs in taking care of the patient population, I would think somebody, if you were running your business, would say, you know, it might make some sense for us to make the investments that can preclude the continued expenditures, since I don't know where the money is coming from.

Senator HOLLINGS. Is there an accepted norm? Since I am here and can ask these questions, is there an accepted norm, by any corporate endeavor, of our growth budget whereby a certain percentage is applied to research and development in order to remain a successful corporation? It certainly would be more than 1 percent.

Mr. DRESING. That is a good question, and just this morning, Hewlett-Packard announced that the products that they have brought to market in the last 5 years have been the result of the 50-percent investments of their total budget. I mean, R&D is a necessary part of any industry.

Senator HOLLINGS. What is Hewlett-Packard's percentage? What percentage was that?

Mr. DRESING. In the last 5 years, 52 percent of the products that were brought to market were developed with the R&D's dollars that were expended during that same period of time. It is a quick return.

Senator HOLLINGS. What percent would Hewlett-Packard be spending on research; would you know?

Mr. DRESSING. I don't know what the total dollar is.

Senator HOLLINGS. In the pharmaceutical industry, they tell me the average expenditure for R&D is 16.8 percent in order to keep the industry going successful, at the cutting edge, in business and everything else like that. I will get some other comparisons.

Mr. DRESING. We could use the gross national product of this country as an example; 13 percent of it goes to health care costs, yet one-third of 1 percent goes to research. Now, those kinds of figures are going to absolutely assure that what we better be doing in this country is going out and finding the dollars that are going to pay for the care of the individuals that we absolutely refuse to address.

NIH has a policy of being able to fund, right now, 1 or 2 out of 10 grants in some institutions versus in the 1970's, when we were funding 7 out of 10 grants, is an indication that not that we are giving better scores or that we have relaxed our standards, but that we are finally getting a return on the investment that we have made in this country to stimualte technology and research to the point where it can provide some return.

What we are saying now is, well, wait a minute, guys. we have brought you to this point. Isn't it wonderful? Look what we have been able to do.

In the Cystic Fibrosis Foundation, we have a gene now for this disease. Finally, we are going to be able to look at this patient population and see how we can alter this disease to stop spending the $300 million that we are spending on that patient population, maybe by solving the disease going out of business.

But now we are saying, oh, wait. No; we are going to cut back the Cystic Fibrosis Foundation research centers by 23 percent next year.

If you take your budget at home, Senator, and cut it by 23 percent, or you take your business budget and without any announcement or previous knowledge, cut it by 23 percent, find out what happens to your efficiencies. I tell you what you are going to do. You are going to shoot yourself in the foot.

Because all of the expenditures that you have made that have brought you to this point are finally looking like we are going to realize a return are going to be wiped out, because we are going to turn out the lights in the laboratories of the people who can bring us to the next stage. Those people, when we turn the lights out, they go away, and they become lawyers and engineers and all the other things in industry that are providing them opportunities to continue career development, and then we are going to say, well, what happened to the 10 questions that we had identified in 1990 that in the year 2000 still are unanswered because we weren't willing to continue putting our money where we knew we were getting our greatest return.

For every dollar that is invested in biomedical research, we get a $13 return. You can't get that in the stock market. That is because we can increase productivity, reduce absenteeism and cut health care costs. If we are trying to balance a budget, if I was trying to balance a budget, one of the things I would look at is: Where can we make investments that are going to provide us with a return that can cut costs in the future, and not think about, well, our grandchildren and our great grandchildren are going to have this great national debt to deal with, and what we need to do is stop spending.

Well, we need to stop spending in some areas, Senator. I have a real problem with the fact that this country is spending $307 billion in defense next year and $7 billion for biomedical research. The NIH budget in its entire 100-year history, would not equal what we spent in defense in the last 2 years. I don't get that, and I don't understand how we are going to ever answer these questions.

Senator HOLLINGS. You sound like my lawyer friend, Mel Bailer. Where did you get the 13-to-1 figure?

Mr. DRESING. The 13 to 1 is a figure distributed by the ad hoc committee, by any of the coalitions who have been able to do the research on seeing what happens when you are able to either reduce the cost by insurance companies for taking care of a problem, the costs of absenteeism, the loss of productivity versus what happens if you are able to keep that worker in the work place as a productive person where you don't have to spend the care on keeping a portion of this population healthy.

Senator HOLLINGS. Is there an authority that I can quote?

PREPARED STATEMENT

Mr. DRESING. We will get it for you.

Senator HOLLINGS. I am questioning it, because I want to fix that in. It is very interesting because that is the kind of talk necessary around this town that is all budgeted. They are going budget crazy. They don't know how to spend money, and how to even get it. I have got a value-added tax. I didn't want to bother them, but we will get to it. We have got to pay some bills; we have got to get some money; get the country going. But I need that authority on how we can really be saving money.

[The statement follows:]

STATEMENT OF ROBERT K. DRESING

My name is Robert K. Dresing and I am president of the Cystic Fibrosis Foundation (CFF). I would like to take this opportunity to discuss the importance of continuing to invest in medical research. In particular, I want to thank you for your investment in cystic fibrosis (CF) research. The recent discovery of the gene and protein that cause CF would not have been possible without your assistance. The collaboration of outstanding scientists from numerous institutions, particularly Drs. Francis Collins, Lap-Chee Tsui and John Riordan, with years of support from the National Institutes of Health (NIH) and the CFF, was essential to bringing about the discovery of the CF gene and its protein.

With these new tools, we have come through the bottleneck into a field where research opportunities are plentiful and the returns can be tremendous. Most significantly, we can foresee the chance to change the future for thousands of people with CF, including my 23-year-old son, Rob.

When Rob was diagnosed with CF in the mid-sixties, the outlook for children with CF was bleak. We learned that the lung and digestive problems caused by this disease threatened our youngest child's chances for a full life. With no control or cure in sight--indeed, with few in the medical profession even looking at this disease--we joined forces with other families to try to bring about a brighter future for our children. The money we raised through the Cystic Fibrosis Foundation and the attention we garnered from the medical field has now given us the satisfaction of working with numerous medical professionals interested in fighting CF. In fact, more than 1000 researchers and caregivers attended our most recent medical conference.

Efforts to stimulate science have brought new medical treatments, better enzymes and antibiotics to people with CF, enabling many

to live longer, healthier lives. Our children and young adults are starting to feel the promise of a future free from this disease. As we near the finish line, we must redouble our efforts to ensure that the cure or control that now appears to be within our grasp is not lost. We are on the threshold of finally offering my son and the 30,000 other children with CF the chance to be among the first generation to survive this disease, rather than the last to die. There is no time to waste.

Our diligence--and yours--in selecting and investing in scientific winners paid off. Now again, we must take bold steps to translate the findings into treatments, bringing these basic discoveries to the patients' bedside. No doubt there will continue to be skeptics who will argue that we expect too much too soon. However, as Dr. Collins observed, "There are those who say 'So you've got the CF gene--that doesn't mean you've solved the disease.' But those are the same people who said we couldn't find the gene in the first place."

However, in order for us to reach the finish line, we need your continued investment in biomedical research. The limited federal dollars available today threaten to undermine the goals of the NIH, one of the most productive enterprises in this country. With the weakening support for the NIH, we face a powerful dam ready to burst--a flood of scientific opportunities that may be washed beyond our reach.

I would like to share now how we are working to address this crisis by collaborating with the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) and the National Heart, Lung and Blood Institute (NHLBI). Our own CFF research centers offer a symbol of the importance of a solid and well-supported framework for bringing research advances and illustrate the wisdom of the public-private partnership. We have learned first-

hand that the sum is much bigger than the parts, and that the results of the research centers are far greater than a group of related research grants. Since your mandate, we have invested more than $27 million in establishing a successful network of centers, nine of which have earned support through the NIDDK and NHLBI during the last three years. Your foresight in channeling these funds allowed the centers to lay the groundwork for identifying the faulty gene and protein.

But now, these research centers of scientific excellence face downward negotiations as high as 23 percent which undermine their very purpose. Centers are forced to let highly trained and committed researchers go; indeed, the basic structure of projects begins to crumble as scientists minimize research goals to offset reduced dollars.

Another crack in the structure of our nation's research programs is the low award rate for NIH-approved research projects. Currently, as few as one in seven of the approved, high-quality projects receives funding--an unacceptable figure that is discouraging even the brightest scientists. Which questions are we willing to leave unanswered through such a low award rate?

The Foundation has tried to fill in these gaps by creating the CFF/NIH Research Award--to our knowledge, the first award of its kind. Now in its second year--at a cost to us of more than $1 million--this program is providing CFF funding for outstanding NIH-approved projects. We are also combining forces with the NIH to create another unprecedented program--a joint request for applications to probe the CF gene and the Cystic Fibrosis Transmembrane Regulator (CFTR) protein.

However, the NIH's strength is also threatened by the lack of support for the Intramural Program--the only program of its kind

in the world. The Intramural Program has always represented all that is best in the nation's biomedical research efforts--indeed, many great CF leaders began their careers at NIH. Once again, we have tried to compensate for inadequate funding by expanding our jointly funded fellowship program. At the same time, we have begun a new education initiative in cooperation with the NIDDK for an extensive NIH lecture series on CF advances and we are continuing to cosponsor joint conferences with the NHLBI, such as our previous cell immortalization conference.

We are not just talking about research investments that will pay off only in the long term; we can expect to see the benefits almost immediately. Many of the researchers currently making headlines are very young--Dr. Francis Collins first conceived of gene jumping as a fellow, and Dr. Lap-Chee Tsui started searching for the CF gene just a short time after earning his doctorate. Indeed, that is why it is critical that we invest now--otherwise, we will begin to feel the repercussions almost immediately. We must invest now in scientific training to inspire young scientists to dedicate their lives to changing the future of this disease.

While the Foundation has tried to respond to each area within the NIH receiving reduced funds, this effort on our part is merely a finger in the dam. Moreover, we must emphasize that we cannot continue to supplement the NIH's programs and support our own research simultaneously. Our efforts to instigate pilot and feasibility projects and to foster young investigators who can bring new ideas and new talents to CF are the backbone of tomorrow's research successes.

To guarantee ongoing research progress, our future depends on strong federal support for the full range of research activities--from basic studies which will probe the CF gene and the CFTR

protein to efforts to develop treatment options. One example of building on basic findings is the drug, amiloride, which has been recently explored for its ability to impact the ion transport abnormality in CF. This drug has shown signs of being able to thin the thick, sticky mucus and help people with CF clear their lungs and avoid infections. The Foundation has also been exploring gene therapy to find ways to replace or correct the CF gene, an undertaking we began even before the gene was identified.

As we move even closer to controlling and curing this disease, funds for clinical research will become even more critical. Hundreds of CF patients are currently participating in trials testing steroids, ibuprofen, and aerosolized antibiotics. Another study focuses on the preventive use of oral antibiotics, prior to costly and damaging lung infections. By helping people with this disease before health problems multiply, this type of treatment could lead to enormous savings.

A strong foundation for research would be incomplete without appropriate studies on animals. Despite the widespread scientific commitment to the ethical use of animals in research, scientific efforts in this country are being undermined by animal rights activists. Headlines show intimidation of scientists and damage to research labs draining millions of dollars from already limited research funds. This movement may be the most destructive force to biomedical research in this century. For CF, this is occurring at a time when we finally have the chance for scientists to develop a transgenic mouse--an animal model which would enable testing of the basic defect and evaluation of new therapies. We urge you to take a leadership role in ensuring that animal research is not stifled by special interest groups who disregard the future of our children.

We cannot expect the federal government to meet every research need. However, proven programs like those of the NIH deserve

your full support. Yet, as a society, we have been willing to jeopardize our investment in CF research and in people's lives. Somehow, every year, we have found $500 million to pay for the health care costs of this disease, but we have not invested more than one tenth of these costs into the future of people with CF--an investment which would also reduce the total health care bill.

We at the Foundation are investing over $28 million this year alone in pushing CF research across the finish line. But your investment is vital. We urge you to support the recommendations of the NIH experts and the National Health Council in providing $11.6 billion to fully meet the current scientific needs at the NIH. At a minimum, $9.2 billion is necessary for the NIH to fully restore funds for research centers and new grants, as recommended by the Ad Hoc Group for Medical Research Funding. We also urge your support now as lost opportunities will be even more expensive to try to recapture later.

My son and the thousands of other adults with CF have managed to survive long enough to experience the success of the discovery of the CF gene; we cannot let them down now. While the Cystic Fibrosis Foundation cannot assume the role of the NIH, we will continue to ask the NIH where we can help. In turn, we ask you to strengthen your investment in our research centers and in the NIH's programs--to redirect support where it can bring the greatest and speediest return: our children's lives.

STATEMENT OF ANDREA DILORENZO, NATIONAL COALITION FOR CANCER SURVIVORSHIP

Senator HOLLINGS. Ms. DiLorenzo.

Ms. DILORENZO. Yes; I am very pleased to be here as part of this debate. I am quite literally a product of cancer research and early detection. I am here as a survivor of three primary cancers, the most recent of which was diagnosed only last December and representing the National Coalition for Cancer Survivorship.

Our group is a relatively new organization, some 4 years old, of about 1,500 individuals and organizations involved with the concerns of the 6 million people in the country living with cancer and the 1 million more, some of whom may be in this room right now, who will be diagnosed in 1990 with cancer.

I am not going to talk about statistics so much because that is really not my forte, but I am telling you that research has played an important role in my own choices that I have had available to me and certainly, in my having the ability to have detection early enough so that I could go on to lead a healthy and productive life.

I have been working full-time each time I have come back from my series of treatments, and I do believe that the kind of commitment that our Nation has made to biomedical research, in my case, cancer research, has made a difference between my being here today literally and not being here.

I will tell you a little bit how that is the case. My first breast cancer 5 years ago was diagnosed through early detection mammography. When I had to make, I was given a choice about treatment. I chose to have a lumpectomy, which is removal of the tumor, and a 6-week course of radiation.

I was able to save my breast. I was 33 years old; it was very important for me. This past December, I was given that same option. My tumor on the other breast was caught early; the doctors felt that they could treat it again with radiation, but 2 years ago, I was diagnosed with an ovarian malignancy. My oncologist was concerned about what is happening with the chemistry of my body, what other factors might be going on.

He had just read a study showing that in some cases, there seems to be a statistically significant difference of the possibility that breast radiation was causing tumors in other parts of the body. I then choose a mastectomy. If I had not had access to that study, I might have chosen radiation again, saved my breast, but I might have been dead in 5 years.

Right now I am trying to determine whether or not I am going to have a followup treatment to my recent breast cancer. It was a local cancer, as I said. Until last year, most local breast cancers were treated with either mastectomy or radiation, and that was it.

Last year NCI put out a clinical alert. They had done studies showing the impact of chemotherapy and hormonal treatment on women who had had local breast cancers. Usually chemotherapy or other followup is only done with women whose cancers had spread or in postmenopausal women.

So right now, of my doctors, one of them is recommending that I take a followup treatment. If I do that, I will lose my reproductive functioning, a very big thing. Side effects in cancer treatment are very severe, still.

Because I have researched now, and some of the doctors previously referred to genetic kinds of breakthroughs that there have been, there has been a test I have been able to have on my tumor which shows its rate of growth, its DNA characteristics and other really important information that will show what my true level of risk is for recurrence.

Do I need to lose my reproductive function to possibly keep living a long life? That is very important information for me to have available to me, and I think that we need to be able to get that information out to more people.

I also think that, and my organization feels very strongly, that we as survivors can help contribute to the body of knowledge in a way that we are not being tapped into right now. For example, we

face very severe medical problems following our treatment quite often, either, as I mentioned, secondary tumors; often leukemia results when people are radiated in their chest and abdominal areas, and we have heart, lung and thyroid problems connected with, certainly, chemotherapy after chemotheraphy.

If there were epidemiological records kept and demographic records kept on people who are living with this disease so that we can put this body of knowledge into the general research, we believe we can help to bring about cures and certainly, to help people live longer lives in terms of being more productive and to have more quality of life.

So I guess the main point I would make is to maintain your commitment to NIH and certainly, to the basic research. I think it does make a big difference, and to put more emphasis on survivorship research, of utilizing the people we know are living with this disease.

We are making gains in many areas to utilize us as part of your research. Also, I feel like I would be remiss if I left without saying as you continue your deliberations, to resolve the health care crisis, that we must find ways to give people access to the system. I am here today because I have an excellent health insurance program where I work and I haven't faced discrimination on my job, but literally, people are dying in very large numbers because, despite information that may be coming their way, they are not able to access the system.

PREPARED STATEMENT

They are going to an emergency room in far southeast Washington when they have tumors the size of grapefruits coming out of their breasts, and this is happening. I have seen them. I think that unless this becomes part of the debate, as well, that we are going to keep trying to reinvent the wheel unless we really focus on this access question. Thank you for this opportunity to be here.

[The statement follows:]

STATEMENT OF ANDREA DILORENZO

Thank you for the opportunity to be present with you today. My name is Andrea DiLorenzo. I am a survivor of three primary cancers -- all diagnosed since 1984. I am here today as a member of the National Coalition for Cancer Survivorship (NCCS) to present my organization's views on the need to strengthen and enhance our nation's cancer research efforts. I bring you special greetings from our President and co-founder Dr. Fitzhugh Mullan, who could not be present with you today.

NCCS represents the concerns of six million cancer survivors in the United States -- and the million more who will be diagnosed this year. NCCS is a member of the National Coalition for Cancer Research, a broad-based coalition of fourteen professional and lay organizations committed to searching for cures for and more effective treatment of cancer through research.

NCCS is a coalition of 1,500 individuals and organizations with tens of thousands of members and constituents in the cancer survivorship movement in the U.S. NCCS members include leaders of cancer survivor community organizations, regional and national cancer-related organizations, and many of the nation's most prestigious cancer treatment institutions, including M.D. Anderson in Houston, Memorial Sloan-Kettering in New York City, Fox Chase Cancer Center in Philadelphia, and Howard University Cancer Center in Washington, D.C.

NCCS was founded nearly four years ago by survivors of cancer, their families, and their caregivers to meet the

ongoing needs of those living with the disease. **NCCS defines survivorship as beginning at the time of diagnosis of the disease and lasting throughout the balance of life.**

The NCCS mission is to communicate that survivors can live vibrant and productive lives.

NCCS is based on the concept of the veteran helping the rookie -- the experienced survivor coaching and supporting the newly diagnosed individual. Toward furthering this end, NCCS supports the work of community groups, national publications, peer networking, and coalition efforts. Many of our activities have been focused on:

- o speaking out about life after cancer diagnosis;
- o promoting cancer information and services on a community level;
- o serving as a national voice for survivors before media, government, and health communities;
- o working to reduce cancer-based discrimination in employment and insurance;
- o providing technical assistance to community hotlines and other community-based survivorship programs.

Survivorship -- A Steady Improvement

I come before you today as a cancer success story. Despite my three diagnoses, I am in the fortunate half of those with cancer who are still alive more than five years following diagnosis. As you may know, the American Cancer Society (ACS) reports that there are currently nearly six million

people living with cancer in our country, three and a half million of whom have lived five years past diagnosis.

As recently as the decade of the 1950s, the five-year cancer survival rate was only 25 percent. That rate has increased steadily over the years to its current overall level of just over 50 percent. During this same period we have seen our government steadily increase its commitment to cancer research. Since we know that during that same period, environmental and other factors have in fact exacerbated the occurrences of many cancers throughout the population, we must give credit to breakthroughs in biomedical research for the steady increase in survival rates.

Progress has been made in the treatments of many cancers, such as many childhood cancers, especially leukemia, and in Hodgkins disease, and testicular cancer. In many others, such as cancers of the bowel, lung, and breast, five year survival rates have not improved dramatically.

We believe that answers are available to prolong the life or to cure those diagnosed with these common diseases. To do so will require that we step up our current efforts, particularly our research efforts. Since one in three Americans will develop some form of cancer in their lifetime, many of you in this room today will be touched by this disease. For those who will be diagnosed, and for their loved ones, I urge you to redouble your commitment to fund the research programs and projects that offer survivors the opportunity for a better and longer life.

Personal Benefits of Cancer Research

I am currently recuperating from treatment for breast cancer diagnosed in December of last year. I was treated with a mastectomy and reconstruction. I am now in the process of deciding, along with my doctors, a possible course of follow-up treatment. While follow-up therapy was usually given to women whose breast cancer had spread, generally it was not for those whose cancers appeared to be local as was mine.

Just last year, however, the National Cancer Institute (NCI) released an alert to physicians throughout the country showing promising results of four clinical trials in the prevention of recurrences in women diagnosed with breast cancer whose lymph nodes showed no spread of the disease. These studies included results from treatment by chemotherapy and a hormone, some forms of which had been used effectively for many years in fighting treatment of breast cancer.

In determining whether I shall choose to have follow-up therapy, I have at my disposal important information -- made available through research -- some of which became available only recently. For example, about fifteen years ago, researchers developed a way to determine the hormonal status of breast tumors. Establishing progesterone and estrogen levels has proven an important component in helping determine prognosis, as well as treatment options. Through the recent introduction of a test called flow cytometry, which assesses the tumor's DNA characteristics, including its rate of growth, my doctors and I have even more specific indicators to help determine my risk level for recurrence.

In the final analysis, this information will be essential as I make a decision that could have fundamental implications on both the length and quality of my life.

Survivorship Research: A Neglected Area

As someone whose entire life has been profoundly affected by my three diagnoses of cancer, I would like to speak directly about a dimension of cancer research that has not been given the resources or attention needed as increasing numbers of people survive the disease -- **survivorship research**. Some may believe that spending money researching the issue of survivorship is trivial compared with the research needs aimed at finding cures. This is not true. We know very little, either epidemiologically or demographically, about survivors. Gathering data and promoting research about survivors can provide a myriad of benefits to those working in prevention and cure, as well as to survivors themselves.

There are two areas I would like to address: <u>biomedical issues</u>, and <u>psychosocial problems</u> encountered by those surviving with cancer.

Biomedical Concerns

While many of us are surviving our cancers, the treatments increasing survival have harsh and lasting effects. Treatments themselves can cause secondary tumors -- new cancers -- sometimes years later. Some forms of chemotherapy are known to cause longterm heart problems. In addition, those treated with massive doses of radiation to vital areas in the chest or abdomen are known to develop forms of leukemia, and lung, thyroid, and heart problems, among others.

These longterm consequences are of great concern to me. Five years ago, when my first breast cancer was diagnosed -- through mammography, I might add -- I chose the breast-sparing technique of lumpectomy (removal of the tumor) followed by a six week course of radiation. Given the size and stage of development of my latest breast cancer, I was again offered the option of lumpectomy with radiation. However, two years ago I was diagnosed with an ovarian malignancy. Because of recent research showing the possible link between breast radiation and secondary tumors in various parts of the body, I worried about the possibility of shortening my life to save a body part. I chose instead to be treated with a mastectomy.

Focusing more resources on the longterm effects of treatment of childhood cancers is also imperative. For example, many cancer treatments are known to adversely affect IQ. Many also cause sterility. Young people growing into adulthood with such impairments may be seriously affected.

Obviously, more research needs to be directed toward the study of the longterm effects of treatments so that searching for effective, yet less harmful courses of therapy will become an important element in overall cancer research.

Psychosocial Problems

Quality of Life Issues

NCCS believes that more issues around quality of life must be factored into the treatment of all cancer patients. Currently, many patients with terminal disease are being

kept alive at very heavy cost to them and to their families. Encouraging those with terminal illness to accept experimental treatment which shortens or brings torment to their lives is an issue which must be carefully scrutinized as treatments are developed.

In addition, longterm survivors have many fundamental issues which they must confront everyday. For many the emotional and psychological scarring that may result in the loss of body parts may greatly delay or prevent resumption of a normal lifestyle following treatment. For others, continuing sexual difficulties or infertility remain problems which affect their intimate relationships and family life.

To be able to effectively confront and overcome these barriers to achieving a high quality life after cancer diagnosis, more must be done to understand the problems with which longterm survivors must cope. More research is needed to help bring these issues to the forefront, and to help those working with cancer survivors have the necessary information and tools at their disposal to offer the hope of a full life. Research on the psychosocial aspects of survival is a natural accompaniment to the continued successes of cancer research. As researchers help us live longer, we survivors can contribute to the body of knowledge about how all survivors can live well with the disease.

Job Discrimination

More than one million cancer survivors face unfair and often illegal job discrimination in this country. Perhaps due to the stigma of the disease as a "killer" and disabler, often

cancer survivors returning -- or wanting to return -- to work are demoted, or out-and-out fired from their jobs. Isolation is also a problem. One member of NCCS, a medical professional, had her office moved into a small, isolated cubby hole following her return from cancer treatment. Research is necessary on the longterm employment and wage patterns of cancer survivors in order to reverse the stigma placed on cancer survivors in the workplace, and to help in the development of just public policy and fairness in employment opportunities.

Barriers to Insurance

The area of health insurance presents one of the most difficult minefields for those diagnosed with cancer. Many face inadequate health insurance coverage which dries up in the middle of their treatment, the loss of insurance coverage following their treatment, or the inability to have their pre-existing condition covered by a new insurer. For cancer survivors, followup treatment and ongoing testing is vital to their health. Losing health insurance can literally mean a death sentence.

Statistics must be collected on the number of people who are so adversely affected by inadequate or nonexistent health coverage. Having this information at our disposal will help us to evaluate the effectiveness of the solutions we develop.

Conclusion

Mr. Chairman and Members of the Subcommittee, I am more grateful than you can imagine at having the opportunity to be with you here today. I and members of the National Coalition for Cancer Survivorship appreciate the support for biomedical and cancer research that Congress has given for

so many years. But, as you know, we as a nation have far to go in overcoming this insidious disease. I urge you to recommit yourselves to funding the research needed to find a cure for cancer, and with that pending, to enable survivors and survivors-to-be to have the opportunity for long and good lives.

As a final message, I would encourage continued funds for cancer treatment research, prevention research, and of equal importance, survivorship research. On behalf of NCCS, I offer our continuing pledge to work with you toward these ends. Thank you again for the opportunity to appear before you today.

Senator HOLLINGS. You are the most intelligent patient I have heard. You understand really what is going on, and I am sorry for the ailment, but if I were a doctor, I would be delighted to have you as a patient.

What you all are talking about is very significant in your area. It was the year before last that the top seven in mammography left NIH and went to Georgetown. They had to change their homes.

Ms. DILORENZO. I am going to see him Friday morning.

Senator HOLLINGS. Is that right? And you are going to Georgetown and not the NIH?

Ms. DILORENZO. That is correct, yes.

Senator HOLLINGS. Oh, my Lord, working for the other side.

Ms. DILORENZO. Sorry.

Senator HOLLINGS. Very good. Thank you.

STATEMENT OF ABBEY MEYERS, NATIONAL ORGANIZATION FOR RARE DISEASES

Senator HOLLINGS. Ms. Meyers.

Ms. MEYERS. Yes, Senator Hollings.

My interest in the biomedical research program is outlined in my written testimony. I have three children with a rare disease called Tourette syndrome. I got into this field against my will, really, in my effort to help my own children and try to understand how the biomedical research program is run in the United States.

In the beginning, we had scientists apply for NIH grants who were turned down for funding on the basis that the disease was so rare that NIH felt they wouldn't be able to find enough patients with the disease.

We were able to overcome this barrier, and with the increasing public awareness of Tourette's syndrome, many, many thousands of people have been diagnosed. It is not as rare as once believed.

But in terms of this committee, we really want you not just to increase the NIH budget, as everybody has come to you every year and asked you to do, but to look at how it is being spent. Because we have some major concerns; 10 years ago, when I came into this field, we were told not to ask for earmarked money for a specific disease because it wouldn't be right. It might work earmarked for one disease but it would be taken away from another disease.

Basically, NORD, the National Organization for Rare Diseases, we don't come before you and ask for money earmarked, but every year we see that more and more diseases are getting those earmarks. We see a pie, a whole pie, and every year, you have been generous and you have increased that pie at least by the rate of inflation. But the size of the slices of the pie are changed by the committee language.

In the beginning, hardly anything was being done for AIDS. Now, the slice for AIDS is just huge. When the slice started growing, the money was taken directly out of cancer research. I want to volunteer that on my own income tax, I will pay the Government an AIDS tax in order to solve the problems of that disease, but please don't take money away from other diseases to fund that initiative.

The next thing is the human genome project. This is a wonderful, wonderful concept, because 3,000 of the 5,000 orphan diseases are genetic, and we want to see them all cured. But we wonder why the human genome program is being run like a baseball program. Every place I turn, every scientist I speak to, every company I speak to tells us that we have to win the race, that we are in competition with the rest of the world.

I really don't think, if you really look at it, that anybody is going to own the results of the human genome project. You won't own chromosome 18, so why should the American taxpayer be shouldering this huge burden and replicating things that other countries are doing?

We are paying an awful lot for this program that should be looked at internationally on a cooperative level. There should be an international agreement that nobody will try to patent any genes or chromosomes. We don't really have to win that; all of mankind is going to be the beneficiaries.

The other issue is indirect costs. I don't think that people in academia are going to appreciate this, but they have gotten totally out of hand, and we have seen this committee over the years try to do something about controlling them. But nothing has been done. But they are beyond belief. The fact that a $100,000 grant now costs the Government $190,000 or $200,000 is not reasonable, because that money, those indirect costs, could fund additional RO1 grants.

So there should be no reason that one university is allowed to charge 90 percent in indirect costs and another one 20 or 30 percent in indirect costs. There has got to be a uniform way of addressing this, because our prime concern is RO1 grants, investigator-initiated research.

There is also a lot of money being wasted. We have found, and there is a report on this from the National Commission on Orphan Diseases which was submitted to Congress last spring, the spring of

1989, which tracked the waste of money, because there is no coordination between the departments of government.

For instance, we have seen clinical trials supported by the NIH, wonderful clinical trials, many of them on orphan diseases because industry can't make a lot of money from a rare disease and so NIH will support these trials, but the people at NIH don't talk to people at FDA, and after spending millions of dollars on doing the study, that data cannot be submitted to the FDA, and so the studies have to be replicated.

We desperately need a central office for rare diseases at the Assistant Secretary's level to make sure that these valuable dollars aren't wasted on efforts like this.

Finally, there are, as Ms. DiLorenzo just said, we looked at research as a long pipeline. The scientist drops, and I hear in one end of the pipeline, and he, for years tracks that research; he has to jump over obstacles all along the way. It is not just funding, it is regulation. For instance, the amount of money that has to be spent this year alone to conform to the animal welfare regulations that were enacted last year, and I heard somewhere it was $1 billion that has to be spent by universities as well as the NIH to conform to these regulations which was just a minority of people in the United States who are pushing for this.

We are throwing that money out. So when you finally get the product all the way through the pipeline, the end result just doesn't get to the patient.

Senator Hollings, I am telling you, many people outside the beltway don't understand this, but patients with serious and chronic diseases do not have health insurance. They cannot get health insurance. We have 10 employees in my company, in the National Organization for Rare Disorders, and I cannot purchase health insurance for them, because they have preexisting conditions.

PREPARED STATEMENT

The health insurance industry is getting away with murder, literally, and so the products that come out of that pipeline from NIH and from industry are not obtainable to people without health insurance. We must have universal access to health care in the United States.

Thank you.

[The statement follows:]

STATEMENT OF ABBEY S. MEYERS

Mr. Chairman, members of the Subcommittee, I am honored to have the opportunity to speak to you today about the importance of biomedical research and the impact it has had on my own family as well as an estimated twenty million Americans afflicted by over 5,000 rare "orphan diseases". An orphan disease is defined under federal law as any disease or condition affecting fewer than 200,000 Americans.

As you probably know, I wear many hats, but my primary role in life has always been a wife and mother of three children. My oldest son was born in 1968, and when he was five years old he exhibited involuntary repetitive muscular movements and unexplainable outbursts of sounds that were bizarre, disruptive and frightening. His teachers punished him, numerous physicians told us the motor and vocal symptoms were "nervous habits" that would disappear if we ignored them, and psychologists delved into our parenting skills trying to determine what we were doing wrong.

After several years of fruitlessly searching for a diagnosis, I happened to read a newspaper article about a young man with Tourette Syndrome. I instantly recognized that my son had the same symptoms, and took the article to our pediatrician. He knew nothing about the disorder; in fact he said, "This is one of those 'Back of the textbook' diseases which we were told in medical school that we would never see".

By the time my son was finally diagnosed as having Tourette Syndrome, he could no longer write, dress or feed himself because his arms swung wildly about every time he tried to make a purposeful movement. Although the Tourette specialist who diagnosed him said Tourette Syndrome was a neurological movement disorder, the text books still categorized the disorder as psychiatric.

The need for biomedical research was very clear. Without research there would be no adequate treatment, and without research the cause of Tourette Syndrome would always remain uncertain.

Subsequently, my two younger children got Tourette Syndrome; my second son when he was 9 years old, and my daughter when she was 23 months old. It was because of families like ours, with multiple cases of Tourette Syndrome, that a genetic component was suspected. I began to work for the Tourette Syndrome Association which tirelessly tried to entice the interest of scientific investigators who would study the disorder. Finally, a geneticist at Yale applied to NIH for a grant, but his priority score was not high enough for funding. The pink sheet for his grant, which contained criticism of his proposal, indicated that the scientific rationale was excellent, but the reviewers felt that Tourette Syndrome was so rare no investigator would be able to locate a sufficient number of Tourette Syndrome patients who would participate in the study.

At that time we knew of 80 Tourette families in Connecticut and another 200 on Long Island who were eager to participate in this study. In time, because we were enraged at the reviewers ignorance of Tourette Syndrome and could prove that their assumptions were wrong, the study was funded and conclusive evidence was gathered to prove that Tourette Syndrome is a genetic neurological movement disorder that is <u>not</u> caused by poor parenting skills, but rather by an autosomal dominant gene.

What did I learn from this experience? As my family lived through the anguish and uncertainty of each day, we thought we were the only ones who had ever experienced years of misdiagnosis, bizarre symptoms and worthless therapies. We soon learned that just about everybody with Tourette Syndrome had similar experiences; practically no one was diagnosed immediately and treatment was a medical game of Russian Roulette with pills and side effects. We later learned that a treatment was available in Europe that helped some people with fewer side effects, but American pharmaceutical manufacturers were not interested in getting the drug approved by the FDA because the small number of people with Tourette in the United States did not represent a viable market.

Speaking to leaders of many voluntary health agencies representing other rare diseases I found they <u>all</u> had similar problems: misdiagnosis, very

little research, unfamiliarity by the public and physicians, ineffective treatments and lack of interest by drug manufacturers was the norm, not the exception. We decided to work together in an informal coalition to pass the Orphan Drug Act. That coalition later became the National Organization for Rare Disorders (NORD). The Orphan Drug Act, which is seven years old this year, has been model legislation that has forged a partnership between government, academia and industry to conquer rare diseases. Today, more than 330 compounds have been designated as orphan drugs by the FDA, and many hopeless, crippling and fatal disorders are treatable now as a result of this legislation.

The 1985 amendments to the Orphan Drug Act created the National Commission on Orphan Diseases. I was privileged to serve on that Commission, which submitted its report to Congress in 1989. For more than two years we studied all of the problems that inhibit progress in research on rare disorders, especially procedures at NIH.

Speaking for the voluntary health sector, I must tell you that there has been, and continues to be a perception that biomedical research at NIH is funded according to the degree of fear the public has about contracting a disease. Among ourselves we speak about the "disease of the month syndrome" on Capitol Hill. The Commission tried to document some of these problems but could not find a difference between the priority scores for applications to study rare versus prevalent diseases. However, a carefully conducted questionnaire of researchers revealed that the great majority of biomedical scientists **believe it is much more difficult to obtain NIH funding for a rare disease project than for a prevalent disease.** As long as this perception exists, it will inhibit research on orphan diseases.

Subsequently, the Commission decided to examine the overall amount of funds that NIH spends for rare disease research annually. We found that in 1987 the federal government spent $1.3 billion for orphan disease research, but **over half** of this sum was spent on rare forms of cancer. There are about 200 rare cancers, but there are approximately 4,800 other rare diseases that share the remaining $640 million. This does not offer much hope to patients who realize that they have a low priority disease.

This year (FY 90) the rare disease community has been devastated by the NIH funding crisis because most Institutes are funding fewer than 20% of approved grants. It seems that every week during the last few months we have heard about scientific investigators (who have devoted their careers to certain orphan diseases), who have lost their funding. In many cases virtually no other scientists are studying those diseases so research has come to a grinding halt. I cannot tell you what it means to have a serious or fatal illness knowing that no research is being pursued, and there is no hope left to cling to. In past years NIH threw orphan disease patients life jackets to keep them afloat in a stormy sea, but this year the government is throwing life jackets that are not inflated, and patients are deprived of any hope to stay afloat.

Many rare disease researchers who have assembled major clinical research projects have lost funding and discontinued their studies. Many are returning to private practice or securing jobs in health related industries. The outcry from the orphan disease community has been intense. In some cases compassionate NIH officials have been able to provide some funding for partial continuation of a few projects, but it will take many years to rebuild the community of academic investigators that we have lost this year.

We deeply regret that thousands of families with hereditary disorders are asking why the government is spending $58.5 million on the Human Genome project while scientists hot on the trail of specific disease genes are losing their funding? They are asking why $1.6 billion is being spent on AIDS when in the absence of new money much of this sum is being taken away from other diseases; and in the voluntary health sector many agencies are now considering if they should demand that NIH earmark funds for their disease since they know that other disease groups have done it successfully despite Congress' resolve not to.

We want you to re-examine how you appropriate funds to NIH, and how NIH is spending those funds. Every time Congress sets aside money for a

biomedical "Manhattan Project", there is less money available for RO1 grants. When new animal welfare regulations were set in place, did Congress consider how much it would cost for every research institution to comply? And how much must be spent on extra security procedures in recent years to protect academia from animal rights activists who intimidate scientists and destroy laboratories with impunity?

Moreover, isn't there some way Congress can control indirect costs for RO1 grants? At some universities indirect costs have doubled the cost of every grant. Few of those dollars directly benefit patients or investigators. There must be some way to develop an equitable system that will cover "reasonable" indirect costs, allowing more grants to be funded on the dollars you appropriate.

Finally, I want to say that I have the deepest admiration for members of this committee. Every year you try your best to increase NIH funding, and every year you are told that more and more is needed. I would not like to be in your "no win" situation. This is why it is time to examine how NIH is spending its funds, what political pressures it is responding to, and whether grants should be funded on the basis of scientific excellence or other standards.

We understand President Bush's budget asks for an 80% increase for the Genome project ($108 million), $75 million has been earmarked for cancer control activities, and 852 grants are reserved for AIDS research, to name only a few set-asides. Meanwhile, 1,000 fewer RO1 grants were funded in 1990 than in 1989. The funds you appropriate to NIH represent a large pie. We in the voluntary health sector watch the size of each slice change every year as focus intensifies or decreases on certain diseases. Needless to say, the whole pie should be made bigger, especially when public health priorities like AIDS and the Genome project are added. While in my heart I would like you to reserve one very large slice of the pie for orphan diseases, I would deeply regret if you took money away from cancer, Alzheimer's or heart research to accomplish this. Conversely, we are deeply disturbed that money is being taken away from orphan diseases to fund research on higher priority diseases.

Therefore, on behalf of NORD, on behalf of the Commission, and on behalf of my children, I ask you to make the NIH funding pie bigger and enable NIH to fund at least 1/3 (5,500) approved RO1 grants. Areas of research that cry out for more attention can attract scientists through RFP's or contract solicitations, not through congressional language requiring certain dollar amounts to be spent on certain diseases. We cannot afford to fund any mediocre grants simply because money has been earmarked and a minimum number of grants must be funded.

If this can be accomplished, NIH will get more research for every dollar spent, and orphan disease investigators will feel that they have an equitable chance to compete for funding. Today, however, their chance is so slim that scientists are reluctant to apply, and this is the crisis we ask you to solve.

Senator HOLLINGS. Good. I wanted you to elaborate when you were talking about controlling the costs. One institution charges 90 percent, you say, in indirect costs?

Ms. MEYERS. That is right.

Senator HOLLINGS. Do you mean in one grant and then the way that they spend their money, is that the sort of——

Ms. MEYERS. It is whole institutes. An institute like Yale or Harvard negotiates an indirect cost rate with the Federal Government, which is applicable to any grant they get, where whether it is biomedical research or Department of Energy, and that indirect cost rate at some of the universities is 90 percent. We have heard that at one university, the indirect cost rates is 110 percent, so a $100,000 grant will cost the Government $200,000 or $210,000. Yet, smaller universities in Arizona and around the country were charging much lower rates, perhaps 30 percent.

So the reasoning is that the eastern universities have higher indirect cost rates because it costs more for people to live in that area of the country, and I certainly agree with that, but there is no reason why there should be such a wide discrepancy and that that money should be spent on the buildings and the facilities of the university when physicians are losing RO1 grants.

Senator HOLLINGS. I understand that my own Medical University of South Carolina has 42 percent, so that is one-half what they are charging.

Let me yield to our distinguished colleague here from Pennsylvania, Senator Specter. Senator, you haven't heard the stimulating panels here with respect to biomedical research. Mr. Dresing here says it is not a priority in this country. With $700 billion in overall health costs that we have paid this year, in 1990, and there is only $7 billion in the budget; we are going out of business.

Senator SPECTER. Thank you very much, Senator Hollings, for inviting my comment. I start by complimenting you for requesting this hearing. This is a special hearing of the subcommittee and, I think, a very important one. I regret that I could not be here earlier, but since 9:30 the Senate has been considering an amendment for an investment tax credit on the clean air bill, and I am the principal sponsor, so I have been on the floor up until this moment.

I share your concern about this issue and I want especially to introduce Dr. Clayton Buck of the Wistar Institute. He is professor of biology at the University of Pennsylvania and the associate director of the Wistar Institute, and he is going to be testifying on this issue.

I think that more of an allocation should be made and that this is a very high priority. We have not made a sufficient allocation considering the opportunities in this field, the inflationary costs and the research scientists who are available to work here but are moving into other disciplines.

It is one of the real problems that we have to address. I am glad to see a hearing on this issue, and I will join you, Senator Hollings, in lending my best efforts to try to find additional funding.

Senator HOLLINGS. We will do our best, and we appreciate it. Let me thank this panel and keep the record open for further questions. Very good. We will move now to our third panel, Dr. Jim Ballenger of the Medical University of South Carolina; Dr. Clayton Buck of the Wistar Institute and Dr. Herb Pardes of the Columbia University Medical School.

Let me yield just a moment to Senator Specter.

Senator SPECTER. Thank you, Mr. Chairman. I appreciate the opportunity to introduce Dr. Clayton Buck of the Wistar Institute to the panel. Dr. Buck is a very distinguished research scientist who comes from one of the most prestigious institutes in the United States, the Wistar Institute in Philadelphia, PA.

I have reviewed his testimony, and he has some very important information to provide to the subcommittee. I regret that I cannot stay, because I have to be at a veterans affairs hearing.

I want to say that Senator Hollings has taken on this hearing in addition to his regular duties as chairman of the Commerce Committee, a committee with substantial responsibilities. We make

more apologies for our abscences than we contribute. I yield my time.

Thank you very much, Mr. Chairman.

Senator HOLLINGS. Thank you very much.

STATEMENT OF DR. CLAYTON BUCK, WISTAR INSTITUTE

Senator HOLLINGS. Dr. Buck, please.

Dr. BUCK. Thank you. Thank you, Senator Specter, Senator Hollings. I essentially am going to sound like the fourth of the Andrews sisters, I think, because much of what I have to say you have heard earlier. I think if you are going to have one take-home lesson, I think it is this: I think that the lack of dependable, long-term funding in basic biomedical grants to individual investigators at the untargeted level in a peer review system is causing us to lose professional personnel; it is causing us to lose students. It will eventually erode the very foundations of the biomedical community at large in this country.

I think you have to keep in mind that, in fact, our entire biomedical community, health care delivery, as well as our new biotechnology industry, is based entirely on this kind of research. I think Dr. Korn said it beautifully, that industry is not interested in how bacteria mate, but out of those kinds of studies has come a whole industry, has come a whole different way of treating patients in hospitals, has come an entire different way of looking at science.

Science is bigger now; science is more expensive now; science is more technologically oriented, and our budgets have not kept up with it. The country has not even given health care delivery, I think, the priorities it should have.

So fundamentally to anything you do, I think, is to increase the amount of funds that go to this untargeted basic research, and that doesn't mean things like the human genome project. I haven't talked to one scientist who favors that. I think that that money is going to be ill spent.

The information we can get from that kind of a project will come from individual people looking at specific genetic diseases. They are already being looked at. If we are going to form a consortium to sequence the entire human genome, then let's sit down with Japan, Germany, France, and England and do it, but let's not finance it at the expense of funding individual research.

I think I have essentially touched all of the points I want to make. With regard to training, I will tell you just a personal anecdote. I have four young physicians from the University of Pennsylvania working in my laboratory. Someone earlier said one of the important things as far as getting basic research into the clinic is having physicians do this research, and that is absolutely true.

For the first time in 20 years, physicians are realizing you don't do research out of your hip pocket. They are sending their young, their best young men back into laboratories to learn how to do it. These are the people who are going to interface basic science and clinical medicine.

I have four people like that in my laboratory trying to get fellowships, looking at what is happening to funding, asking questions about what is happening in the future. One of them said, "I don't have a future." He is now running the pulmonary unit at a major

hospital in Philadelphia. Two others are trying very hard to get fellowships so they can continue.

PREPARED STATEMENT

The point is that these people have to get support. Nobody goes into this business to make money; they go in to create ideas. I think this lack of funding is affecting our young people enormously, and I think that is the take-home message I want to give you.

Senator HOLLINGS. Good.

[The statement follows:]

STATEMENT OF DR. CLAYTON BUCK

I am Dr. Clayton Buck, Wistar Institute Professor or Biology at the University of Pennsylvania, and Associate Director of the Wistar Institute, a free standing research institute founded by Casper Wistar in 1892. Thank you for the opportunity to testify before you today, and, more importantly, for your vital commitment to the medical research programs which led you to convening this special oversight hearing.

The biomedical research funding crisis has been approaching for a number of years during which funding has increased at a little over 4% per year, while the actual inflationary cost of research is over 10%. This budgetary short fall, and the lack of any plan for continued adequate support for biomedical research will, if not soon corrected, have a negative impact on our Nation's health care delivery system. At the present time, the lack of funds are seriously jeopardizing our research efforts in three crucial areas:

* the foundation and future growth of basic biomedical research;
* the infrastructure of our biomedical research facilities;
* the education and training of young physicians and researchers.

Research Foundation

We have experienced a scientific revolution during the late 70's and 80's. We can now think in terms of using genetic manipulation to diagnose and treat diseases. We can begin to think in terms of correcting genetic disorders. Our knowledge of cancer viruses and AIDS has suggested new insights into neurological disorders. We can think in terms of gene therapy for diabetes, Parkinson's disease, and immunodeficiencies. Our knowledge of molecular structure can now be applied to developing new agents to prevent blood clotting and to fight atherosclerosis. We now have the probes to investigate the molecular basis of emphysema, asthma, chronic neurological diseases and perhaps even aging. It is

possible to begin to understand embryonic development at the molecular level which should eventually lead to ways for preventing certain birth defects. Similarly, we are beginning to understand how the brain functions and how the nervous system is assembled; knowledge essential if we are to begin to reverse permanent nerve damage, or correct neurological disorders. We have come a long way, we have farther to go.

These enormous advances over the past two decades in this country are due primarily to our support of individual investigators engaged in basic biomedical research in the colleges, universities, medical schools, and research institutes throughout the Nation. This "untargeted" or basic research, supported by peer reviewed grants to individual investigators, has provided the foundation of knowledge upon which our current health care system is built and will serve as the foundation for our entry into the 21st Century.

Without this reservoir of knowledge, we could not have mobilized our current assault on AIDS, developed new diagnostic procedures for genetic diseases, come up with new therapeutic strategies for cancer, or developed the non-invasive imaging producers currently in use across the country.

Unfortunately, this foundation is now threatened. On the average, 75% of the approved grants go unfunded, and about half to a third of the applications ranked as excellent to outstanding are not being funded. Further, the research that is funded is being cut -- through downward administrative adjustments negotiations - to the point that the research progress is seriously hampered. Work that could be accomplished in three or four years, now takes five to seven. Much work has to be delayed or go unfunded.

Research centers, where much of this work is conducted, act as unique resources to bring together scientists from different

disciplines. Such an arrangement allows multiple groups of scientists to work collaboratively, using common biotechnology facilities and sharing costly equipment. The budgets of research centers are cut on the average of 13%/year, and relatively little new funding is available to take advantage of exciting research opportunities which are constantly emerging. In response, centers are being forced to turn to the corporate world for financial support. American corporations are so committed that many research institutions are being forced to seek funding from the European and Japanese commercial sectors. Investments by foreign companies in American research do not come without strings attached. Collaborative research agreements with foreign companies obviously give such companies an advantage when it comes to capitalizing in the marketplace the fruits of the research efforts supported under these agreements.

However, the impact of funding shortages goes far beyond the laboratory and the research scientist. The lack of funds to allow the Nation's scientists to continue to explore these complex areas of biology will be costly in terms of the quality of life for millions of people -- to say nothing of the lives lost. In 1991, we will be spending $660 Billion on health care costs and less than $8 billion on the research to control and eradicate disease. The alternative to supporting research opportunities is high cost hospital care and the inability to respond to unexpected medical crisis such as AIDS.

Medical research is good for our Nation's citizens, and for our economy as well. The entire biotech industry is a result of our investment in basic research. It has created jobs, saved lives, nurtured future research, and contributed to our international competitiveness. The profitability of our pharmaceutical industry which is challenged from abroad argues strongly for the development of new areas of biotechnology. Dollars spent on research are a wise investment, the fruits of which accumulate in the years ahead. We should use this time of

great opportunity to re-think our commitment and strengthen our research foundation.

Infrastructure

Our research infrastructure is inadequate to meet the complexity of the research studies presently being supported. As our knowledge base has increased, so too has our sophistication in the conduct of research. However, we are facing tremendous problems which need your attention and support.

* The equipment in most institutions is aging rapidly. Most was purchased over 20 years ago and continues to be used around the clock. New instrumentation required for protein sequencing, DNA sequencing, structural studies, molecular imaging is prohibitively expensive, and yet is essential for modern molecular research.

* With the exception of minor programs to support efforts in animal and AIDS research, no significant funds to make the necessary repairs and renovations to existing facilities have been available, and many Universities and research institutions have been strapped to find funding to bring their laboratories in line with crucial safety and regulatory requirements. In addition, for at least a decade, there has not been any funding for a facilities program to support new construction.

Research Training

The lack of adequate funding for research grants is not only resulting in a depletion of our knowledge pool, but also will most certainly result in a loss of the creative individuals, through lack of training opportunities, required to expand biomedical research. The lack of funds is resulting in the closing of graduate training programs at major universities. There are no funds for fellowships to these individuals. Likewise, postdoctoral

training is drastically curtailed. It is now difficult to impossible to attract postdoctoral fellows outside a few major research centers. The funds for fellows are cut from research grants, and no training funds are made available from other sources.

Further, constraints act as a disincentive for young talented individuals to enter or to stay in the medical research field. It is estimated that by the mid-1990's, 60% of our research training needs will not be met. This is coming at a time when there is an ever increasing demand for research training for bright you physicians who are the future faculty of our medical schools. When research scientists with excellent credentials are being denied research funding, we stand to lose the generation of scientists that come behind them -- for if the mature and seasoned researchers are unable to get funding, how can the young scientists whose research is exciting but not yet mature be assured of funding?

The result is that we are now training many fellows from China, Japan, India and Europe. This is because either these individuals have funds from their own government to support their stay in the U.S., or they are taking the place of American students who have chosen alternative careers leading to more lucrative positions in the business community.

In conclusion, the shortage of funds and the lack of long term planning on the part of the Federal Government has impacted negatively on our biomedical community at all levels. This has come at a time when we should be reaping the benefits of past investments and moving into biomedical frontiers that were once unthinkable. Everyday, we come closer to extending the life of more cancer patients, we have more insights into vascular disease, we understand a bit more about chronic neurological disorders, we come closer to being able to correct genetic disorders and new therapies based upon our more sophisticated knowledge of molecular structure are within reach. It is negligent to stand idle while

our best scientific minds are engaged in efforts to raise money rather than in efforts to cure disease, or while our most talented young people turn to other careers because the future of a career in biomedical science is extremely tenuous. Anyone who has had a member of their family recently diagnosed with a fatal, yet possibly manageable disease knows the urgency and humane importance of expanding our funding of biomedical research so that we can provide hope for our citizens and those of the world.

STATEMENT OF DR. JIM BALLENGER, MEDICAL UNIVERSITY OF SOUTH CAROLINA

Senator HOLLINGS. Dr. Ballenger.

Senator SPECTER. Mr. Chairman?

Senator HOLLINGS. I will yield if you have any questions.

Senator SPECTER. No; I do not have questions. I will leave staff here, and I will review the transcript. Again, I express my regrets and my appreciation.

Senator HOLLINGS. We will be working on it. Thank you.

Thank you, too, Arlen.

Dr. Ballenger.

Dr. BALLENGER. My perspective comes as a former NIH researcher and now a university researcher in trying to run an institute of psychiatry and substance abuse, and it is from that point of view I am testifying.

Senator HOLLINGS. Your statement in its entirety, all three of the witnesses, will be included in the record.

Dr. BALLENGER. Thank you. I will try to shorten what I might have otherwise said.

Senator HOLLINGS. Yes.

Dr. BALLENGER. The first message about our field has to do within our 100-plus year history of psychiatry and substance abuse, the last decade has been without a doubt the most productive. We are now poised at a time in America. If we do the right thing, we can benefit greatly.

The benefit really is a large one in our field for two reasons that are different from some other fields, say, cancer, for instance. Our field has a very large constituency that needs the progress from the research. Easily 10 percent of American public every 6 months has a major life disabling psychiatric problem. It may be 15 to 18 percent. In a life time, it is one-quarter to one-third of the American public has a major psychiatric problem of the nature of a very severe recurrent depression, manic-depressive illness, very severe anxiety problems substance abuse problems, alcoholism, cocaine abuse, and schizophrenia, those kinds of life-disabling illnesses.

The other thing that is different about our field is that we are in a makeup situation. The last 10 years has been wonderful, but prior to that the stigma associated with our field has kept funding away, has kept researchers away, and that needs to be reversed. I have a few thoughts about that. I will give you one example, one analogy. I actually this it is not exaggerating to remind you of the

polio situation, where people spent great time, effort and money taking care of polio victims waiting for the effect of the vaccine.

It is a message that scientists will always bring to you. I will give you one example in my field of the kind of return on the dollar, as you were talking about earlier. We had, prior to the discovery that lithium was an effective treatment for manic depressive illness, manic \depressive illness affects 2 to 3 percent of our population with an illness that occurs 8 to 10 times in their lifetime and takes as much as a decade out of their life.

The development of that one medicine, which I understand costs less than $2 million to develop, between $1 and $2 that NIH spent, that, in the last 17 years, has saved at least $12 billion, which is more money than the Government has ever spent on all of psychiatric research since NIH was founded, that kind of return that we are talking about.

In the substance abuse field, which affects about 8 percent of our population, we have to do some balancing, I think. There has been, for instance, in the prevention area, we have spent about $1 billion recently, and we have made a big impact on the so-called recreational or casual use in the general public. That has gone down.

As wonderful as that decrease is, the use in the addicted populations hasn't changed at all. That is because we in our field believe that people with addictive disorders have, among other things, a genetic vulnerablility to, potentially, a life time of addiction unless interrupted.

I think what we need to do is to balance the efforts we are spending in treatment and in prevention with new moneys to study the problem with effective clinical research that is rigorous, to look at what the effective treatments are and to develop new treatments, because the treatments we currently have that I confront as a clinician are distressingly similar to the polio situation.

We struggle very hard, and 25 to 35 percent of alcoholics are able to maintain a substantial change in their drinking patterns, only one-third. If you look at IV heroin abuse, a very bad illness, only one-third of them are still absent 1 year later. So the progress we need in that area is extraordinary.

I need to emphasize something that is not often understood in the psychiatry field, and that is that the basic research underlying the clinical research is what needs to be actually in catch-up. To give you an example, the brain mechanisms underlying the craving mechanisms that lead to the vicious drug abuse situation, there are real strong leads in that area now and certain brain chemicals like dopamine, medicines can affect that and affect the craving and maybe interrupt the horrible cycle.

Another good example is the work going on in the cocaine receptor. We are getting close to finding the protein in the brain, in fact, where cocaine fits in and leads to all of its mischief. If we can do that, it is a relatively simple scientific measure to find an antagonist that blocks the effect of cocaine.

We do that in animals in the lab. If we develop that, we then can have an antagonist we can use in humans which people could take voluntarily or even a judge could ask them to do it take it, and any subsequent cocaine use would just be blocked, and the problem

would have the kind of revolutionary changes that would save money and difficulties that are obvious.

The kind of scientists we need to get into psychiatry and into substance abuse research, it has been hard to do. The M.D.-Ph.D. is exactly the kind of person, because our questions are really quite hard and very basic. We need mechanisms that help in that regard.

I actually want to tell you three areas I think we really need to work on and then make three suggestions. There are three areas that have just evolved to a point where if we don't take advantage of it, it is a foolish, bad investment.

One of them really does have to do with the genetics issue, and if the genome project was done and all of the work, however it is done, that genetic work will have more impact or as much impact in my field as any other. We need to be ready to do that, and we have not had the help to gear up to do that.

The revolution in the brain imaging that is relevant to my field, the positron revisions from the CAT scan, tells my field for the first time in history what it needs to know about the brain. We don't need to know about x rays, because we don't have to deal with brain tumors and scars.

What we have to do is deal with brains that don't work right, and the CAT scan, for the first time, gives you a functional idea, it gives me a functional idea of what is wrong in the brain. So in the last very few years, we have let CAT scans tell us that there are abnormalities in the brains of schizophrenics. We knew that all along; that there are different abnormalities in people when they are depressed and when they are manic and with severe anxiety disorders like obsessive compulsive disorder and in alcoholism, that kind of area needs tremendous help.

Mostly those projects have been done in a single university or one here and one in Europe. We need a much greater effort. Similarly, for the first time in our 100-year history, we are learning the mechanisms of the brain which will allow us to develop drugs.

Dr. Busch talked about that, too. In the psychiatry field, it is at least as important as it is in the cancer area, and we need the same kind of effort that was done in cancer to be done in my field. I will just give you two reminders of how big the problem is. One-half of all the beds in the world, hospital beds, are filled with people who have the illness schizophrenia, that one illness, one-half the chronic beds. If you take the medical surgery acute beds, hospital beds in the world, 50 to 70 percent of them are occupied with people who have the one illness alcoholism and all of its ravages afterwards.

If we could even develop medicines that were even partially effective in each of those two syndromes, the impact, from a financial as well as human viewpoint, is just really very obvious.

There are sort of three suggestions. We have bantered around here today about the amount of money. I clearly agree with everybody else. We have got to spend more, and I will tell you two things about it. In the sixties, we spent about 2.9 percent of our health care costs on this interprise. It has drifted to 1.5 now.

So the amount of external grants, I think it is important to remember, we need, almost all of us agree, to do research at the

NIH, in that big campus in Bethesda, and we need to do it out in the universities. It is a complementary thing.

There are some things to do at the NIH, but the NIH is doing OK. They need the salary thing fixed and things like that. What is not doing OK is what Dr. Buck and others have said, is the people, the army of people out here who need to do the research.

The young person going into research 20 years ago was told he had a 70-percent chance that if he worked with his mentor, his grant would be funded, and that is a pretty good deal. Somebody who is smart and has all these degrees, they think can win in the game 7 out of 10 times. Twenty years later, what we tell them and which when they hear, they go scoot off to economics and law, is that, look, you have about a 1 in 10 or a 2 in 10 chance of getting a grant, but I am sorry to tell you that who you are competing with are all these gray beards who have been funded for 20, 30 years, and they are the real pros in the world, so you are not competing with the other new person. You are competing with them and all of these people who need to and who have a very natural advantage, and they should keep funded.

That sort of discouragement is really tremendous. So if we went back to spending 2.5 of our health care costs, you talk about some industries spending 16 percent; many spend 5 or 6 percent and say, that is good enough. If we went back from 1.5 to 2.5, we could fund about 50 percent of the grants, and that is a game where to my son, I could say, yes, I think maybe you ought to do that.

He tells me he thinks he should go into law because it is just too hard. I think he should go into this work because it is good work, but it is just adverse at this point.

I think the second thing that, in my field, that is so clear to me, just this last week, I just remembered, as I was sitting here thinking, I lost two young psychiatrist researchers, one in child psychiatry. Even though there are less than three dozen full-time researchers, three dozen, people who do child psychiatry research and one in schizophrenia, after they came out of NIH research training fellowships, both of them went into private practice, because they looked at these things and added it all up and said, You know, on odds, that is just too dangerous a career.

We need to reverse that. I think a 50-percent funding rate would reverse that, but I think we need to do other things, too, and one of the things is I think we need to pay some attention to the issues of how you get funding other than RO1 individual grantings, because at this 11- to 20-percent funding rate, it is very, very hard for young people, and so it is very, very discouraging.

I also finally would make a suggestion that I think it may be time, I think it is time for us to consider a suggestion which is being actively discussed in Washington at the highest levels now, and that is to further the complementary relationship of the intramural NIH in Bethesda, which is so strong, with something like many NIH's outside, satellite types that are based on the same model.

The NIH model is a wonderful model. It puts clinical programs, clinical researchers and basic researchers head-to-head across the hall, and they really interact well with each other, and they provide very efficient research, maybe because they don't have to

spend so much time writing grants. But that is part of what is good about it. But that model can be exported judiciously with interactions between the scientific leadership and the government leadership to take advantages of opportunities that exist in some places that don't exist in other places.

PREPARED STATEMENT

Just to give you an example of how that might work, just in recruiting, if you talk about recruiting patients, if you are going to devote one of these satellite facilities to the study of schizophrenia, for instance, you probably ought to put it where there really are a lot of people with that illness, much more, than, say, in the Washington facility. The same thing with young trainees and the same thing with senior scientists, whose recruiting stream could be a lot more economic.

Senator HOLLINGS. Good.

[The statement follows:]

STATEMENT OF DR. JIM BALLENGER

I am delighted to be able to testify about the opportunities and challenges currently facing the psychiatric, mental health, and substance abuse fields and to suggest mechanisms of Congressional response. The hard-earned progress of the past decade in my field has put psychiatry in the position such that appropriate and significant resources could produce major improvements in the quality of life for a substantial group of Americans. Recent epidemiologic surveys of the US population have documented that at least 10%, and probably 15-18%, of the American public suffers serious and life-disabling psychiatric illness in any six-month period. These primarily involve to the disorders of schizophrenia, manic-depressive illness, anxiety, substance abuse, and various dementing disorders. The relatively lower emphasis on these illness in recent medical research actually places the large psychiatric and substance abuse populations in the best position to benefit from the recent, explosive advances in the neurosciences. However, certain problems have emerged in the past 5 to 10 years which interfere with the realization of this promise, and I would like to comment briefly on some of these issues.

My research career began first at the National Institute of Mental Health and continues now in a University Department of Psychiatry which is also responsible for clinical and research training, clinical care of patients, and the generation of new research findings which will hopefully result in new and improved treatments. From that perspective, I will share with you briefly my ideas about what is needed to support the critical growth of psychiatric research and to highlight those areas in which increased attention will result in rapid progress. This is certainly the most productive time of my specialty's 100+ year history. However, we need a great deal more research, and especially a great many more researchers to realize the extraordinary benefits of this progress. The importance of medical research is clear to Congress, and I would simply remind you of one example, i.e., the heroic efforts and tremendous expenditures which were involved in the care of polio victims prior to the discovery of an effective vaccine. The general public and even Congress may find it more difficult to see an analogous set of issues in the fields of mental health and substance abuse disorders. The development of lithium as the first effective medication in the treatment of manic-depressive illness has conservatively been estimated to have saved at least 12 billion dollars. This amount saved far exceeds that spent on <u>all of psychiatric research</u> in the United States since the NIH was established.

Despite our best efforts to prevent substance abuse and the expenditure of over one billion dollars to support these prevention efforts, we have been able to reduce the consumption of illegal drugs only in the general public, not the addicted populations. Reduction of this so-called recreational or casual use is extraordinarily important, but it has served to highlight how unresponsive are the addicts whose drug

use has continued in an unabated fashion. We believe these statistics highlight the harsh reality that this type of drug use occurs in people with substance abuse disorders who are often genetically vulnerable to serious and potentially life-long addictions to drugs of abuse.

There is a distressing parallel which can be drawn between the efforts of caregivers of polio victims to the situations we, as clinicians, encounter every day in the care of substance abuse patients. As you remember, heroic efforts were offered victims of polio in terms of physical therapy and iron lung support after the illness had done its damage. Given no better choices, we currently apply our best treatments for alcohol and drug abuse again with, too often, disappointing results. It appears now that even with treatment, fewer than 25-35% of alcoholics are able to maintain a substantial change in their drinking pattern. In our best treatment programs for IV heroin abuse, fewer than 35% of addicts are abstinent at one-year follow-up. It is my belief that we need to balance our expenditures in prevention and treatment with new monies for extensive clinical research to determine which treatments are really effective and to develop new and better treatments. These clinical research efforts need to be complemented by an extensive expansion in basic science research of brain functions which underlie drug craving mechanisms and other abnormal responses to alcohol so that the vicious relapse cycle of drug abuse can be interrupted or ameliorated. An excellent example is the current work studying brain mechanisms underlying craving for cocaine and the work being performed to define a cocaine receptor in the brain. Were we able to define a cocaine receptor in the laboratory in animals, it would be relatively simple scientifically to develop an antagonist for this receptor which would block the activity of cocaine. This could rapidly lead to markedly more effective methods of dealing with the cocaine problem in that patients could voluntarily, or even involuntarily through a court process, be given the antagonist which would block any effects of subsequent cocaine use and therefore interrupt its pleasurable/addictive cycle.

Basic science research into this type of problem is critical and one of the areas that requires more attention and resources. The problem of underlying brain mechanisms in complex psychiatric problems requires sophisticated and direct research. There have been very few MD/PhD scientists who devote themselves to full-time research in these areas, and it is this type of scientist whose work will focus on these important areas in an effective way.

One issue that may be difficult to appreciate is the difference between the types of brain research performed by psychiatric and neurological researchers. Psychiatry needs the type of brain research that psychiatrists perform, rather than the type that neurologists tend to be interested in. For instance, neurologists tend to look for the defect in the brain in diseases like Parkinsonism or multiple sclerosis.

In the psychiatric field, however, the strategies are unfortunately very difficult and complex in that they require sn exploration of issues like how a genetically inherited vulnerability can interact with the environment to produce the subtle changes in behavior, thinking, and emotions which result in psychiatric disorders. For instance, how does vulnerability to panic disorder inherited by a young person interact with the loss of a significant relationship to produce an over-reactivity of the brain alarm reactions and devastating panic attacks? Many panic disorder patients then self-medicate with alcohol in an effort to deal with these severe, and often debilitating, anxiety attacks. What are the biological mechanisms involved in this transition? Another recent example from the NIMH is Dr. Daniel Weinberger's work in primates which illustrates this complexity. Dr. Weinberger has demonstrated what appears to be markedly decreased activity of certain parts of the frontal regions of the brains in patients with schizophrenia.

However, these abnormalities were not discovered until an extensive research program in primates demonstrated that these defects could not be observed until a complex abstract task was demanded of the primate, and subsequently the human. In a similar fashion, recent work has demonstrated that the group most vulnerable to the subsequent development of alcoholism is the male sons of male alcoholics. Recent research demonstrates that these young men, prior to any experience with alcohol and certainly before the development of alcoholism, handle alcohol differently. Their brain and metabolic responses are different from that seen in normals, and it is this type of research which should lead to a clearer understanding of how alcoholism develops.

WHAT DO WE NEED TO DO?

I suggest to you that there needs to be a dramatic increase in support, now, to expand the efforts in areas of extraordinary promise. For instance, the efforts which are underway at the NIH to map the human genome will be at least as important to psychiatric and substance abuse disorder patients as in any other area of medicine. Work in the mental health and substance abuse fields needs to be radically expanded to be ready to take advantage of this extraordinary scientific achievement. We also need to immediately expand our work with the extraordinary new brain imaging techniques, magnetic resonance imaging (MRI) and especially positron emission tomography (PET). These techniques allow radically improved pictures of the brain and ongoing brain function and are beginning to revolutionize psychiatry. The PET scan has already demonstrated basic brain changes between states of depression and mania in the same patient and in the brains of patients with obsessive compulsive disorder and panic disorder. However, I think it is important to realize that these observations have been generally made only in one research group or research facility, and the capabilities in this area need to be radically expanded if we

are to realize the promise of these new advances in a timely way. We are also beginning to understand the mechanisms involved in the development of new medications in the psychiatric and substance abuse field and attention here could medically improve our ability to treat patients previously unresponsive to treatment.

AREAS NEEDING IMMEDIATE EMPHASIS

- Neuroimaging, especially PET to follow-up abnormalities observed in schizophrenia, depressive disorders, obsessive compulsive disorder, panic disorder, and alcoholism.
- Genetics. An intensive search for biological markers of vulnerability to drug abuse, and major psychiatric disorders needs to be performed and linked to the attempt to systematically map the human genome. Cell lines from families with high prevalence of mental illness need to be developed as well as the identification of families with high prevalence of mental illness.
- A more extensive program to develop effective new psychotropic medicines to treat substance abuse and major psychiatric illnesses would be highly effective now. For example buprenorphine holds promise as a treatment for opiate addiction as well as do fluoxetine and carbamazepine. These leads need to be rapidly explored. Similarly, the new class of antipsychotic agents typified by clozapine which are effective when all other antipsychotic agents fail in schizophrenia needs to be rapidly explored. Efforts comparable to those expended on drug development in the cancer field are currently necessary in psychiatry and substance abuse and hold remarkable promise.
- Basic science studies of the receptors for cocaine and marijuana are critical.
- Studies of the effects of illegal drugs (especially cocaine) and alcohol on the developing fetus and the implications of prenatal exposure for future behavioral abnormalities or increased susceptibility to substance abuse.
- Further studies of brain lesions in the hippocampal region leading to abnormalities in schizophrenia and in patients with memory disturbances.
- Rapid follow-up of the possibility of transplanting fetal cells into adult brains to "repair" brain lesions.
- Studies to identify how primary psychiatric disorders lead to substance abuse disorders. For instance, how do panic attacks in a panic disorder patient lead to alcohol or cocaine abuse?

- Research into the psychiatric disorders in children, an area that has been terribly neglected. Just a few years ago, there were fewer than two dozen full-time psychiatric researchers in the field of child psychiatry. There is great promise for both psychiatric and substance abuse disorders in children if we devote sufficient energy and resources to this area.

- Similar efforts need to be made in the large chronic psychiatric population which comprise 40-50% of the nation's homeless.

WHAT RESOURCES ARE NEEDED?

We need a substantial increase in funds devoted to the area of general medical and bioscience research. In the 1960s, we were devoting approximately 2.9% of health care costs to research, but this figure has slipped to 1.5% in recent years. This needs to be returned to something like 2.5%, which would allow approximately 50% of approved research grants to be funded. At this point, only 11% of approved and excellent applications to NIH are actually funded. This results in demoralization in the field, and the potential loss of an entire generation of young researchers, just at the time when they are most needed in this field. Significant efforts also must be made to maintain funding stability such that careers can be built and sustained. In addition, I think we need to explore mechanisms which will reverse the discouragement currently experienced by young researchers in the field. Recently, I lost two researchers who had both been through NIMH research fellowships for several years and who were ideally suited to contribute to the markedly underpopulated research areas of schizophrenia and child psychiatric disorders. However, the current climate led both of these young and extremely promising researchers to choose private practice instead of research careers. I would strongly suggest to you that we cannot afford to lose even a single well-trained and talented researcher in these fields, given their central importance to our society. I would challenge Congress to work with the field to develop new mechanisms that will successfully stabilize and expand the research enterprise and to support the appropriate growth of the psychiatric research community. This community has always been small relative to the task at hand. However, at this point in our history, and especially given the tremendous need, it is remarkably small. This is especially true in child psychiatry and this needs to be corrected as quickly as possible.

I personally feel we need to approximately double the amount of money devoted to the funding of research grants so that we can fund approximately 50% of approved grants. I also feel that it is critical that we develop new mechanisms to complement the excellent but extremely competitive individual grant RO1 process. We need to find ways not only to foster new and excellent research but also the careers of

young researchers. These mechanisms should have dual goals of both the advancement of knowledge in an individual project but also to develop new psychiatric researchers.

Given the remarkable progress possible in the field but the relatively underdeveloped research cadre and research infrastructure, considerable special attention needs to be paid to mechanisms which successfully develop and support successful psychiatric research groups. We need programs which would put senior mentor researchers together in stable situations with groups of young trainees so that careers are carefully nurtured and protected more than is presently possible in this currently discouraging environment.

I would offer the specific suggestion that we explore the establishment of smaller research facilities outside of Washington, but modeled along the lines of the National Institutes of Health. The NIH model of putting clinical care programs together with dedicated clinical research and basic research programs has been demonstrated to be extremely effective for the advancement of clinical science. I would cite only the fact that papers from the NIH research groups are quoted three times more frequently than papers from extramural researchers. Essentially, not only do we often get better research out of the dedicated NIH groups, but we clearly also get a more efficient return for our dollar. The interaction of clinicians, clinical researchers, and basic researchers is extremely stimulating and efficient, in part because it is removed from the laborious and extremely time-consuming task of planning and writing grant applications.

As a former NIH researcher who is now in a university department, I believe some of the advantages of the intramural NIH setting can be exported in smaller "mini-NIH's" to great advantage if they were centered around clinical and research facilities and positioned to take advantage of certain local opportunities. For instance, many of the clinical psychiatric research issues require large populations of patients which would be much more readily available in particular sites outside of Washington. Also, a steady stream of trainees could be recruited and even supported through local mechanisms. One of the major issues at the NIH is the low salaries that are offered compared to competing universities. This problem also needs to be corrected at the NIH, but the satellite facilities I am suggesting could immediately offer a better salary range and would be able to attract and support both senior research mentors, young trainees, and researchers early in their careers.

These research facilities could be carefully planned to maximize their effectiveness and should be more focused in their efforts. For instance, they might well concentrate on the study of a particular problem like schizophrenia or Alzheimers. I have recently developed plans for such a center to study the basic and clinical research aspects of substance abuse and am convinced that such a satellite "mini-NIH"

would be highly successful, being able to perform certain tasks even better and in a complementary fashion to the National Institutes. Such institutes could be developed in concert with leadership at the national, Congressional, and scientific levels and therefore be unusually dedicated to identified priority areas. The development of these facilities in such a collaborative manner would also greatly increase their chances of success.

I would suggest that there be immediate exploration of this particular model because it seems to respond to many of the stresses and strains of our current system and to hold considerable promise for rapid progress. Its advantages include easier access to large patient populations; more flexible funding mechanisms following university rather than federal guidelines; natural and ready establishment of research careers both at the senior mentor level and at the younger trainee and early researcher level; and a geographic spread which would stimulate more rapid and appropriate attention to these problems across the country.

SUMMARY

Psychiatric and substance abuse disorders are the most common health problems faced by our society. The research personnel and infrastructure to take advantage of the remarkable current situation in neuroscience is too small and needs specific attention. There is an overwhelming, almost immediate need to develop a more favorable climate for larger numbers of highly qualified scientists to make career decisions to concentrate on these disorders.

To accomplish these goals, I suggest that increased funds need to be immediately directed to this effort and new mechanisms of support need to be developed during this "catch up" period. In particular, I am suggesting that mechanisms outside the usual single investigator stimulated RO1 research grant need to be developed. My principal suggestion is that we develop smaller research-oriented institutions in appropriate locations across the country. These research facilities would take advantage of opportunities in the local setting, but would utilize the very productive "NIH model" in which clinical facilities are coupled with dedicated clinical researchers and basic researchers. These "mini-NIH's" could focus on a particular research problem or population, e.g. schizophrenia, substance abuse, etc. These centers could provide the necessary stable research funding and infrastructure and therefore increase the efficiency of the scientists. Perhaps even more importantly, they could serve as training sites for an expanded research force which is critical to our ability to take advantage of the remarkable opportunities we now have in the mental health field, and to deal effectively with the most prevalent disorders of our society.

STATEMENT OF DR. HERBERT PARDES, COLUMBIA UNIVERSITY MEDICAL SCHOOL

Senator HOLLINGS. Dr. Pardes.

Dr. PARDES. Senator Hollings, I would like to first thank you for your leadership, because we really need people who will take the lead in government in biomedical research.

Senator HOLLINGS. You can see the tremendous interest that we have got. We have good interest in this one. I am supposed to have been on the floor at 12 o'clock, and I apologize. I am listening. Go right ahead.

Dr. PARDES. I am vice president and dean of the Medical School of Columbia. I was a former NIH Director, so I know it from the inside here, and I am president of the American Psychiatriac Association.

There is simply an enormous disparity between the promised opportunities of science today and the resources. Biomedical research is one of the few areas in which the United States really still retains leadership. Other countries have seen this, and they are going after it. Japan has targeted biotechnology as the key technology of the future. Four other countries have passed us dramatically in terms of the amount of civilian R&D they have put up over the gross national product in the last 15 or 20 years.

The United States has been in the lead, but it is declining. There is deteriorating physical plant; there is deteriorating equipment. You have heard about the decrease in numbers of young people. In fact, we at one point were training some 16,476 people supported by NIH. That was in 1969. That is reduced now to 12,000, from almost 17,000 or 16,500 down to 12,000.

You have heard about the salaries. This is not exactly a plush career that we are preparing people for. There is no space in academic centers, despite marvelous and flourishing technology. There is no place to put people, and one of the big problems there is there is no clear target for money in order to support the necessary refurbishing and expansion of the physical plant.

Other facts which pertain here, are that the United States in 1961 through 1980 introduced about 23 percent of all the new biotechnology products. Japan at that time was producing less than one-half of that. We have reversed. Japan has again taken over the lead in this regard. This is not only important for health, which is the most critical issue here, but also for foreign trade, for domestic jobs, for international leadership.

Federal funds available for purchase of academic research equipment and technology has declined 78 percent between 1966 and 1983. You have heard the discussions about very few grants being funded. There are answers with regard to the approval rate, I must say. The reason for the high approval rate is: No. 1, that science has gotten extraordinarily better; the competition is keen, so you are getting the best people and putting them forward, but also the staffs at the Institutes actively discuss with potential applicants whether they should come in or not.

So a lot of grants that might have come in otherwise have been discouraged, so you have got a larger pool in there. It is not that we haven't added to the budget, and it has been the leadership of you and many others that has enabled us to do it. It is that we

haven't added enough to meet the opportunity in a bold fashion with appropriate boosts.

We have seen the need in the other areas. In the last decade, the annual increase was something like 3.6 percent for NIH in constant dollars for research. In defense R&D, in contrast, it went up 81 percent.

When I was at one of these hearings presenting to Senator Rudman, he at one point to me said, "Doctor, did you want $5 million for that program or $5 billion?"

I said, $5 million.

He said, "Doctor, excuse me. I also serve on one of the defense committees." [Laughter.]

Senator HOLLINGS. I serve with him. Right.

Dr. PARDES. We need an increase proportional to the opportunity, not just a debate about whether we exceeded inflation by 1 or 2 percent. If we don't get it, we are going to lose this critical window; a lot of people won't get into the pipeline, and you can't make it up easily later.

We need a signal to people in science or contemplating science that we are going to make this a major priority.

What to do? No. 1, give NIH the boosts recommended to $9.2 billion, an added amount of $1.2 billion; launch a program to provide necessary support for equipment and the refurbishing of our laboratories. We have great scientists. We have got to have decent places in which they work.

Increase the support of young scientists; increase the number of young researchers who are training. That drop is extraordinary, from 16,500 down to 12,000;

Protect the science from regulations that block us and add enormously to our costs, such as some of the animal care regulations;

Announce to the public that we are not going to give up the leadership in biomedical research, that the country is going to make it a top priority to support biomedical research and launch an all-out effort to keep our science first-rate and make the understanding of causes and the development of cures much more likely to happen for this country.

I might say that I serve as a dean of a medical school, and my days daily are characterized in the following way: One gets news of an extraordinary piece of science that people are working on, ways of taking a look at abnormal genes, putting them in animals and seeing how they cause diseases, but we need new facilities. We need new equipment.

Where do we get it from? People will come in and say, we have a specific way, in terms of gene mapping, of finding the genes that cause brain diseases. Again that requires new technology and new space. A young person in my place comes in, excellent, puts in a grant, gets a top priority score; he doesn't get the grant; he is now leaving to go to private industry.

We need a new science building to put some of our scientists in. There is no place to go. Private benefactors don't want to put money into buildings. There is no place for us to go for that kind of support.

The scientists' grants get cut, and you have heard of these so-called downward negotiations. They are into the dean's office for additional moneys.

Somebody made some comment about overhead costs. Overhead costs are an important part of research. You can't do research in a tent. Some of those costs help with the heat, the lighting, dealing with regulations, the grants and contracts officer, the buildings and the maintenance of buildings. One of the problems is that we are so constrained. If I could leave you with one major message, Senator, is that I applaud your leadership, and what is needed here is not the simple year-to-year 1 percent or 2 percent above inflation increase.

We need to recognize that there is an extraordinary opportunity, and if we don't take it, Japan, West Germany, and France will take it, and the question is: Where do we want to be in the world in terms of science, and how will that affect the health of our people?

Senator HOLLINGS. I have really got to run. I will run, and I apologize.

I will only make one little correction quickly. Dr. Robert Elsner, of Alaska University, was down on the ice at the South Pole the year before last, and he is doing research in a tent. [Laughter.]

It is a three-layer cloth tent. He has got his little computers and everything else and what they call a Weddell seal, and he wires up his seal and lets it go down in the hole in the ice, which is 35 feet thick, by the way, down into the sea there at the South Pole. The seal goes down at 300 to 500 meters, stays down for 1½ hours, collapses its lungs and stops its heart, according to that computer, and after staying down there for 1 or 2 hours, comes back up to get his fish to eat, reinflates his lungs and restarts that heart to beat again.

In sudden infant death syndrome, the SIDS malady, he is finding out why is it advantageous to sustain for a seal but death for the human, and he is doing it in a tent. I thought you would like that story.

PREPARED STATEMENT

Dr. PARDES. Just tell him that if we don't get any more money, I will be joining him there shortly. [Laughter.]

Dr. BALLINGER. Thank you very much.

[The statement follows:]

STATEMENT OF DR. HERBERT PARDES

Good morning, I am Dr. Herbert Pardes, Vice President for Health Sciences and Dean of the Faculty of Medicine of the College of Physicians and Surgeons at Columbia University. I am also President of the American Psychiatric Association and former Director of the National Institute of Mental Health. I speak on behalf of the almost 10,000 people working at the academic center at Columbia as well as the 36,000 membership of the American Psychiatric Association and believe I convey the views of the thousands of people involved in biomedical and behavioral research as well as many countless numbers who benefit from the fruits of that research.

I come to tell you, Senator, of a disturbing disparity between the promise of our research efforts and the reality of current funding. Academic health centers are experiencing constrictions for support in all directions. Reductions in reimbursement for health care allow less in the way of any support of the service sector for areas where service and research overlap. The absence of money for capital projects in general contributes to the erosion of the capital plant for science. In many states a general economic downturn constricts available money for health, education and research.

To compound this, the direct constraint of support for biomedical and behavioral research has created an acute situation for support of health research. The Administration's current proposed 4.7 percent increase is below the NIH's projection of 5.9 percent for the biomedical research and development pricing index in FY 91. When one separates out AIDS research and the human genome initiative the increase is reduced to 3.7 percent and is even below the Administration's 4.2 percent estimates for overall inflation in FY 91.

In FY 90, "downward negotiations" reached their peak for all time with average cuts of 12 percent for noncompeting research project grants and 13 percent for competing awards. The FY 91 request assumes reductions of 10 and 14 percent respectively.

These cuts make it increasingly impossible for first class research to be performed. The research cuts proposed are widespread with cuts in research centers, recommended cuts in BRSG monies, etc.

Biomedical and behavioral research is important for many reasons. Research is one of the few hopes people with serious illness have for relief. I am sure you are aware of the enormous number of vaccines, treatments, new technologies that have extended life, and relieved pain and suffering.

But one can see advances from research that go beyond the effects on human suffering. Health reasons are one of the main causes for decreased productivity in the work place. Alcoholism, depressive disorders, chronic medical conditions of varied sorts, all undermine the potency of our nation's industrial effort. Thus, a healthy work force is important for a healthy economy.

Further, it is tragically well known to all of us that we are in a dangerous situation in terms of the decline of American leadership in a whole host of industries. Biomedical research is one of the major remaining enterprises in which the United States has leadership. To cut the legs out from the scientists in the United States and make them unable to compete with the rest of the world runs the risk of handing over leadership in this industry as well to others.

It is troubling to realize that the United States is proceeding in a different direction from other leading countries of the world in

terms of support for civilian R&D. Whereas in the early sixties the percentage represented by our civilian R&D of the over all GNP, was about 2.7 percent, today, that percentage has dropped to about 1.7 percent. In roughly the same time frame at least four other countries have gone in the reverse direction moving from a percentage of about 1.7 several decades earlier to a figure currently about 2.7 to 2.8 percent. Do we want to allow to happen here what has happened in some other industries?

It seems to me there is every reason for us to insure full funding of medical research in this country. We spend $2,000 per person on health care expenditures annually and only $30 - $35 per person on research to prevent and cure disease. While NIH has only increased some 3.6 percent per year in the last decade in constant dollars in research, the defense R&D has increased 81 percent in roughly the same period. Currently, we are funding less than one out of every four approved research grants. While we were funding some 16,476 research trainees in 1969, the level supported today has dropped to 12,020. Also stipend and tuition levels are not being increased to adjust for cost of living increases or restoration of the cuts resulting from last year's sequestration.

We are not bringing researchers into lucrative careers. After seven years of college the research trainee receives only 17,000 as a stipend and then when finishing his or her period of traineeship enters a research position which pays about $31,000.

Our research facilities are in trouble and need major restoration as has been reported in a number of major studies. In 1988 a study by the National Science Foundation and the NIH reported that 45 percent of medical schools surveyed described their facilities as inadequate to support their medical research program needs. There has been a failure to address this problem and a constant erosion of the medical research capacity. Ultimately this simply defers and increases the cost to restore. For every $1 spent on construction in 1987 $2.50 was deferred. For every $1 spent on repair and renovation, $3.60 was deferred.

We urge an improvement of support for NIH and ADAMHA that fits the needs. The $9.2 billion figure for NIH would allow 30 percent of grants to be funded, would allow a full $56 million to go to BRSG, would allow an adequate increase in research training support. In an analogous fashion a $1.2 billion figure for ADAMHA, would allow ADAMHA to fund 30 to 33 percent of their grants and a more adequate support for research training.

I have seen the problems right within a medical center. We are losing our best young people. They watch the developments and pull away as they see their scientists, mentors and colleagues run into trouble in support. This country has certain basic values which includes being responsive to people in need, trying to stay economically and intellectually strong, and being thoughtful in terms of those efforts which accomplish many ends, i.e., human compassion and economic productivity.

The opportunities are enormous. We have determined ways by which the AIDS virus penetrates the cell and are working on techniques to thereby block its invasion. We are working on the mechanisms of memory deterioration with the hopes that we can develop treatments and prevention methods that reduce the number of Alzheimer's patients being institutionalized, we are working on better and better technology to identify early lesions within the brain, heart, body in general to provide earlier detection of cancer and heart disease. We are working to understand transmitters and receptors to develop better techniques for preventing drug abuse and psychiatric disorders.

All of these efforts require money, people and adequate facilities. I plead with you to make these available and sustain the sense of vitality in our nation's biomedical research effort.

Thank you for your ongoing leadership and your attention and response to my comments.

CONCLUSION OF HEARING

Senator HOLLINGS. You win. Thank you all very, very much. The subcommittee will stand in recess subject to the call of the Chair.

[Whereupon, at 12:20 p.m., Wednesday, March 28, the hearing was concluded, and the subcommittee was recessed, to reconvene subject to the call of the Chair.]

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